

Epidemiological Evaluation of Dupuytren's Disease Incidence and Prevalence Rates in Relation to Etiology

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Abstract Dupuytren's Disease (DD) is a common, fibroproliferative disorder affecting the palmar surface of the hands which is often irreversible and progressive. Understanding the epidemiology of DD is important in order to provide clues to its etiopathogenesis. This review aims to evaluate the epidemiological studies carried out in DD since 1951. Studies evaluating the epidemiology of DD were searched using Medline, Pubmed, and Scopus which dated back from 1951 to current date. Inclusion criteria were any studies investigating the prevalence or incidence of DD in any population group. A total of 620 articles were cited. Forty-nine studies were subsequently identified as relevant to evaluating the epidemiology of DD. The prevalence of DD in all studies increased with age with a male to female ratio of approximately 5.9:1. Prevalence rates ranged from 0.2% to 56% in varying age, population groups, and methods of data collection. The highest prevalence rate was reported in a study group of epileptic patients. Although, only one study calculated the incidence (as opposed to prevalence) of DD to be equal to 34.3 per 100,000 men (0.03%). In conclusion, the prevalence of DD in different geographical locations is extremely variable, and it is not clear whether this is genetic, environmental, or a combination of both. The majority of the prevalence studies have been

conducted in Scandinavia or the UK, and the vast changes in population structure, the changes in prevalence of associated diseases, and the change in diagnostic criteria of DD makes understanding the epidemiology of this condition difficult.

Keywords Dupuytren's disease · Epidemiology · Etiology · Prevalence

Introduction

Dupuytren's Disease (DD) is a common, fibroproliferative disorder affecting the palmar surface of the hands which can present itself as a clinically challenging disorder for the patient and the surgeon alike. The disease is often progressive, irreversible, and commonly bilateral. DD can be a psychosocially and physically disabling condition which can also have a significant impact on healthcare economy [65]. It is, therefore, considered important to time surgical operative intervention appropriately [45, 59]. The disease is thought to involve abnormal tissue contraction, shown to be mediated by the myofibroblast in the palmar fascia causing a digital flexion deformity [101]. Therefore, knowledge of the exact causation of DD may provide clues to mechanism of DD as well as other fibrotic disorders. In addition, understanding the epidemiology of DD is important in order to provide clues to its etiopathogenesis.

By looking at the medical literature, it soon becomes apparent that the epidemiology of DD has been previously studied extensively albeit only in limited geographical areas [23]. There has been a much quoted concept of DD being labeled as the "Vikings" or "Nordic" disease. Other than the common prevalence of DD in Scandinavia, no objective scientific evidence has been found to date to support and substantiate the "Nordic" origin of the disease.

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In addition, with the exception of a high prevalence rate in Northern European communities, no actual genetic factors have implicated DD as having arisen in the Scandinavian population [23, 29]. The global presence of DD in most countries suggests that the origin and spread of the disease was much earlier than previously speculated and patterns of migration have led to a hypothesis that DD is a genetic disease [69].

DD is found to be most prevalent in Northern European Caucasians [8] where it is one of the most commonly inherited connective tissue disorders with a prevalence reaching 30% in the Norwegian population aged over 60 years [15]. In contrast the prevalence rate of DD is reported to be just over 4% in the male population in England [26]. These particular prevalence rates have been quoted in many previous epidemiological studies.

DD is a condition which has been linked to many risk factors including a history of smoking [14], alcohol consumption [77], frozen shoulder [95], epilepsy [71], diabetes mellitus [6], carpal tunnel syndrome [11], history of manual labor [21], and hand injury [47, 68]. All of these reports are controversial and frequently delivered based on selective data. Factors associated with increased severity include male gender and a young age at onset, which are often reported although the evidence appears to be weak [45]. With an evolving population these prevalence values may or may not be accurate in relation to the present day. It is likely that the population structure will be quite different today than that of 50 years ago. Increasing changes in the environment, working patterns and social structure may also have a greater impact on the observed changes in the epidemiology of DD.

This review aims to assess in detail the epidemiology of DD since by evaluating all published literature with reference to DD epidemiology. The knowledge gained from this review will provide better clues to the reported epidemiological trends, relevance of genetic and environmental factors as well as associated factors implicated in the evolution of this enigmatic disorder.

Identification of Epidemiological Studies

Studies evaluating the epidemiology of DD were searched using Medline and subsequent cross referencing to earlier articles. The following keywords were used to cite relevant articles: Dupuytren's, disease, contracture, history, population, prevalence, incidence, and epidemiology. The search included all case reports, letters, communications, prospective, and retrospective studies. Inclusion criteria were based on incorporating any study investigating the prevalence or incidence of DD in any population group. Studies were excluded if they limited their data to a known DD cohort.

A total of 620 articles were cited and reviewed. Forty-nine studies since 1951 were identified as relevant studies investigating the epidemiology of DD. A relevant study

was one that calculated a prevalence or incidence rate of DD. These studies were categorized as cross-sectional, longitudinal, observational, review, or cohort, and the results tabulated (Table 1). The study setting was noted, e.g., to see if patients were examined as inpatients or outpatients. In addition to this, the data collector and the person who examined subjects were tabulated to enable evaluation of accurate disease diagnosis.

Prevalence or incidence rates for each study were tabulated and, where possible, compared between males and females with reference to age groups within each population. Familial aggregation which has been confirmed in DD [69] is considered to be important in relation to the epidemiology of DD; therefore, heritability data was explored in each study. Risk factors (e.g. diabetes and smoking) for DD investigated in each study were also examined and tabulated.

Review of Significant Studies

The 49 studies identified and tabulated (Table 1) in this study dates back from 1951 to 2008 covering a range of countries from North America to East Asia and Australasia (Fig. 1). Forty-one studies were cross-sectional studies with three cohort, two longitudinal, one observational study, one questionnaire survey, and one review. The prevalence rate was calculated in 48 studies with only one study presenting an incidence rate, where numbers of new cases of DD were calculated over a period of time. The incidence rate of DD for the British population in 2004 was calculated as 34.4 per 100,000 men between the ages of 40 and 84 years with a gradual increase in incidence with increasing age [48].

In order to better understand the distribution of the disease, our findings were further subclassified into age and gender. Prevalence rates of DD ranged from 0.2% to 56% in varying age groups and depended on methods of data collection. The prevalence of DD increased with increasing age, a similar finding in many studies (Table 1, Figs. 1 and 2). The highest prevalence rate (56%) was seen in a study group of epileptic [19] patients.

Geohagan et al. in 2004 calculated the prevalence of DD for patients between the ages of 24 and 97 years of age in the West Midlands, UK [35]. The prevalence rate for a population of 383,000 was 0.2%. This, however, was not based on clinical examination of every subject but was dependent on the coding for DD within general practice databases. Although it included both sexes and all ages, it provided little information on the distribution of the disease. This may have been due to the fact that the coding was not done accurately as the coding term and coding numbers were not specific enough. We know that in the UK, there are a number of different generic codes for DD including the umbrella term musculoskeletal disorders.

Table 1 Population studies.

Author	Date	Geographical Location	Study Design	Data Collector	Prevalence or incidence rate			Age group		Presence of heritability	Significant risk factors
					Total	Male	Female	Male	Female		
Herzog EG [43]	1951	North England	Cross-sectional study of 1,434 manual laborers and clerks	Author	4.25%	–	–	>40 years	–	No mention	No significant difference in prevalence of DD in manual workers (4.5%) and clerks (3.8%). No mention
Gordon S [38]	1954	Canada	Cross-sectional study of 2,705 hospital inpatients	Author	–	33%	–	66–75 years	66–75 years	No mention	No mention
Yost J [105]	1955	New York, USA	Cross-sectional study of 5,062 hospital inpatients	Author	3.4%	2.3%	2.3%	37–100 years	37–100 years	One case with definite family history—early age at onset in offspring. No mention	No significant correlation with hand trauma.
Hueston JT [46]	1960	Australia	Cross-sectional study of 3,700 people in community	Author	–	23%	22%	>60 years	>60 years	–	No mention
Early PF [26]	1962	Lancashire, UK	Cross-sectional study of 6,979 people in community.	Author	3.5%	3.8%	2.3%	15 to >75 years	15 to >75 years	–	Strong association between epilepsy. No relationship between DD and manual work. No mention
Mikkelsen OA [74]	1972	Haugesund, Norway	Cross-sectional study of 16,000 inpatients	Author/ Surgeon	–	9.4%	2.8%	>16 years 70 to 74 years = 36.8% (max prev') >75 years	>16 years 85 to 89 years = 25% (max prev') >75 years	–	–
Critchley EM [21]	1976	Preston, UK	Cross-sectional study of chronic epileptics	Author	56%	57%	56%	35 to >75 years	35 to >75 years	–	Link to anti-convulsants to DD due to peripheral stimulation of growth factors
Stuhler T [24]	1977	Germany	Cross-sectional study of 524 epileptics	Author	21.6%	–	–	–	–	Genetic aspect must be taken into consideration	Idiopathic epilepsy is most associated with DD
Ravid M [43]	1977	Israel	Cross-sectional study of 959 diabetics	Author	17.6%	–	–	–	–	–	Increased risk of DD in older diabetic patients
Mackenney RP [61]	1983	Coiswolds and Chilterns, England	Cross-sectional study of 919 patients attending the orthopedic clinic	Surgeon	–	5%	3.5%	–	–	–	Positive correlation between stretching of palm and DD
Arafat M [4]	1984	Manchester, UK	Cross-sectional study of 392 patients with Rheumatoid Arthritis (RA)	Rheumatologist	6.4% with RA, 16% without RA	7.6% with RA, 16.1% without RA	5.7% with RA, 15.9% without RA	30 to >70 years	30 to >70 years	Genetic factor in RA as a protective factor against DD?	No mention
Noble J [78]	1984	UK	Cross-sectional study of 273 diabetic patients	Authors (physician and hand surgeon)	18% when examined by physician, 42% when examined by hand surgeon	25% when examined by physician, 41% when examined by hand surgeon	13% when examined by physician, 42% when examined by hand surgeon	>16 years	>16 years	–	Increased risk of DD in diabetic patients

Table 1 (continued)

Author	Date	Geographical Location	Study Design	Data Collector	Prevalence or incidence rate			Age group		Presence of heritability	Significant risk factors
					Total	Male	Female	Male	Female		
Egawa T [28]	1985	Japan	Cross sectional study of 3,383 patients attending orthopedic clinic	Author	1.8%	-	-	40–59 years	40–59 years	No mention	No mention
Laplaine D [51]	1985	France	Cross-sectional study of 197 epileptic patients	Author	8%	-	-	-	-	No mention	No evidence to suggest increased risk of DD in epileptics.
Stewart HD [98]	1985	UK	Cross-sectional study of 235 patients with Colles' fracture	Author	6.8%	-	-	18–86 years	18–86 years	No mention	Mild disease in patients who developed DD after fracture. No DD progression after 20 months.
Patri B [82]	1986	France	Cross-sectional study of 155 patients	Author	9%	-	-	20–90 years	20–90 years	No mention	Increased prevalence of DD with increasing age
Guitian AQ [42]	1988	Spain	Cross sectional study of 1,455 undergoing general medical examinations	Author	9.9% 25.5%	-	-	45–54 years >75 years	45–54 years >75 years	No mention	No mention
Eadington DW [24]	1989	Edinburgh, UK	Cross-sectional study of 266 type 1 diabetic patients	Author	24% smokers	-	-	36–84 years	36–84 years	No mention	Increased risk of DD in diabetics and smokers
Egawa T [93]	1990	Japan	Cross sectional study of 1,154 nursing home patients	Author	-	19.7%	9%	Over 60 years	Over 60 years	No mention	No mention
French PD [33]	1990	London, UK	Cross-sectional study of 50 male AIDS patients	Genito-Urinary Physician	-	6%	-	23–56 years	-	No mention	No significance of HIV on DD.
Bower M [13]	1990	London, UK	Cross-sectional study of 50 male HIV infected patients	Physician	-	36%	-	19–54 years	-	No mention	Significant impact of HIV on DD.
Eadington DW [25]	1991	Edinburgh, UK	Cross-sectional study of 200 type 2 diabetic patients	Experienced observer	24%	-	-	36–84 years	36–84 years	No mention	Increased risk of DD in diabetics and in smokers
Thomas PR [100]	1992	Middlesbrough, UK	Cross-sectional study of 500 claimants with vibration white finger.	Author	13.6%	-	-	>45 years	>45 years	No mention	Positive correlation between DD and vibration white finger.
Arafat M [3]	1992	Manchester, UK	Cross-sectional study of 484 patients in 2 epileptic centers	Author	12% and 38% 44%	13% and 44%	11% and 28%	<30 to >70 years	<30 to >70 years	No mention	Increased prevalence of DD with increasing age. No evidence to link DD and epilepsy
Noble J [77]	1992	Manchester UK	Cross-sectional study of 50 patients with liver disease	Author	28%	-	-	<30 to 70 years	<30 to 70 years	No mention	Increased risk of DD in patients with liver disease
Kelly SA [47]	1992	Derby, UK	Cross-sectional study of 235 patients with Colles' fracture	Author	8.5%	-	-	47–79 years	47–79 years	15% had a positive family history	25% consumed large amounts of alcohol; 5% taking anticonvulsant
Lennox IAC [52]	1993	Aberdeen, Scotland	Cross-sectional study of 200 nursing home patients over 60 years.	Author	30%	39%	21%	>60 years	>60 years	No mention	No mention

Bergenudd H [10]	1993	Malmö, Sweden	Longitudinal study of 574 people in community	Author	6%	10%	2%	55 years	55 years	No mention	Non except poor peripheral pulses.
Bovenzi M [12]	1994	Italy	Cross-sectional study of 570 quarry drillers and stone carvers	Author	10%	–	–	Mean age—39 years	–	No mention	Increased risk in vibration exposed manual workers
Renard E [88]	1994	France	Cross-sectional study of 120 diabetic patients	Author	35% type 1, 30% type 2 diabetes	–	–	–	–	No mention	Increased prevalence of DD in diabetics
Chammas M [18]	1995	France	Cross-sectional study of 120 diabetic patients	Author	35% type 1 diabetics, 28% type 2	–	–	–	–	No mention	Increased prevalence of DD in diabetics, risk increases with longer duration of diabetes.
Arkilla PE [7]	1996	Finland	Longitudinal study of 207 type I diabetic patients	Author	4%	–	–	21–39 years	21–39 years	No mention	DD risk increases with patients age and duration of DM.
Dasgupta AK [20]	1996	India	Cross-sectional study of manual workers	Author	4%	–	–	>21 years	–	No mention	Vibration exposure increases risk of DD.
Arkilla PE [6]	1997	Finland	Cross-sectional study of 139 type 2 diabetic patients	Author	14%	–	–	49–73 years	49–73 years	No mention	DD risk greater in diabetic patients. Prevalence equal in males and females.
Gudmundsson KG [41]	1999	Reykjavik, Iceland	Cohort study of 2,165 inpatients	Physician	13.3%	19.2%	4.4%	45–74 years	45–74 years	No mention	Significant association between DD and manual work, smoking, fasting glucose level.
Gudmundsson [40]	2000	Reykjavik, Iceland	Cohort study of 1,297 males in the community.	Physician	–	19.2%	–	45–74 years	–	No mention	Negative association between DD and joint complaints.
Kilian O [49]	2001	Germany	Cross-sectional study of 172 patients with shoulder pathology	Author	2.9%	–	–	–	–	No mention	Similar histology in DD and frozen shoulder
Smith SP [95]	2001	UK	Cross-sectional study of 58 patients with frozen shoulder	3 surgeons	52%	–	–	Mean 54.9 years	Mean 54.9 years	7% of people with DD had first degree relative with DD.	Increased prevalence of DD in frozen shoulder patients
Omari A [79]	2001	UK	Cross-sectional study of 75 patients with frozen shoulder	Author	1.3%	–	–	–	–	No mention	No mention for DD
Finsen V [31]	2002	Finmark, Norway	Cross-sectional study 456 people in community.	Surgeon	7.5%	11.9%	1.5%	>50 years	>50 years	Higher prevalence in family members in same niche	No mention
White HA [103]	2003	Wales	Observational study of 197 inpatients.	Physician	6.6%	–	–	19–101 years	19–101 years	No mention	No mention
Ardic F [5]	2003	Turkey	Cross-sectional study of 78 type II diabetics	Author	21.8%	–	–	46–70 years	46–70 years	No mention	Diabetes is risk factor for DD
Zerajic D [108]	2004	Bosnia	Cross-sectional study of 1,207 people in community appearing to look over 50 years.	Medical student	25%	31%	16%	>50 years	>50 years	No mention	Significant higher prevalence in diabetics.
Geohagan JM [35]	2004	West Midland, UK	Cross-sectional study of 383,000 GP patients.	GP	0.2%	0.15%	0.05%	24–97 years	24–97 years	No mention	Diabetes is a strong risk factor for DD

Table 1 (continued)

Author	Date	Geographical Location	Study Design	Data Collector	Prevalence or incidence rate			Age group		Presence of heritability	Significant risk factors
					Total	Male	Female	Male	Female		
Khan AA [48]	2004	Oxford, UK	Review of National Morbidity Survey of 502,493 men	GP	Incidence rate 34.3 per 100,000 men	-	-	40–84 years	No mention	No mention	
Godtfredsen NS [36]	2004	Denmark	Cohort study of 7,254 subjects	Trained nurse/med student	11%	16%	7%	20–93 years	No mention	Alcohol and smoking risk factors	
Logan AJ [56]	2005	UK	Questionnaire survey of 1,100 climbers	Patient	19.5%	19.5%	-	23–93 years	No mention	No mention	
Burke FD [16]	2007	UK	Cross-sectional study of 97,537 miners	Trained doctors	8.1%	8.1%	-	25–99 years	No mention	Increased risk of DD in diabetics and increased age	
Lucas G [58]	2008	France	Cross-sectional study of 2,406 male civil servants.	Physician	-	8.8%	-	Mean age 50.7 years	20% had family history of DD	Manual work exposure appears to be associated with DD	

Six studies [16, 26, 45, 58, 73, 99] related the epidemiological findings to the heritable nature of the disease. Finsen in 2002 noted that there was a higher prevalence of DD in family members living within the same geographical area as their diseased relative. A further genetic component of relevance to the epidemiology of DD was noted in the cross-sectional study from Manchester, UK carried out in 1984 which examined the hands of 392 patients with rheumatoid arthritis [4]. This study noted that there was a significantly reduced prevalence rate of DD in those with a diagnosis of rheumatoid arthritis, suggesting a genetic protective factor against the disease [4]. Yost in 1955 identified one family of DD with a comment on the development of early age at onset of DD in that familial case [105].

Various studies have examined the epidemiology of DD and also attempted to solve its etiological mystery. Herzog [43] in 1951 and Early [26] in 1962 concluded that there was no significant difference in the prevalence of DD in manual and non-manual workers. A similar result was concluded by Yost [105] in 1955 with a negative correlation between DD and hand trauma. Contrary to these findings, Gudmundsson [40] in 2000 concluded a significant association between manual work and DD while Thomas [100] in 1992 found a positive correlation between vibration white finger and DD. A more recent study to determine whether DD is more prevalent from repetitive trauma found that rock climbing increases the risk of disease development [56].

A similar scenario exists in the prevalence of DD and HIV infected patients, with conflicting data on the significance of HIV in the etiology of DD [13, 32]. There was found to be a high prevalence rate of DD among HIV infected patients. There is however more consistent data in the findings for a link between DD, diabetes mellitus and epilepsy, with many studies finding a higher prevalence of DD in the diabetic population [5, 18, 24, 25, 78, 87, 88, 103, 108]. We compared the prevalence of DD in global epileptic (Fig. 5) and diabetic cohorts (Fig. 6) and found all studies showed a positive correlation between DD, epilepsy and diabetes.

We compared the prevalence rates of DD in different parts of the world (Fig. 2). Studies compared, were ones which calculated prevalence rates for various age categories. Of the seven studies compared, the highest prevalence in males was seen in Bosnia and in Canada for females. The high numbers of affected individuals in both of these studies suggest the diagnostic criteria may be different. Generally the prevalence of DD increases with age (Figs. 2 and 3). From all the reported studies the prevalence in males and females is similar up to 45 years of age after which the rate is significantly greater in males (Fig. 3).



Figure 1 Prevalence rates of DD across the globe.

Prevalence Rates Calculated in a Clinical and Community Setting

Of the 49 studies evaluated, 12 were conducted in a hospital setting, two examining the prevalence rates of DD in a nursing home, and 37 studies carried out in the community. Studies carried out in the nursing home identified a higher prevalence rate of DD compared to those in a hospital or community setting. Prevalence from the community studies on the whole identified a higher prevalence rate than those conducted in a hospital setting (Table 1). The exception to this was the study conducted by Geohagan [35] in 2004 where a very low prevalence rate was calculated.

The differences in the findings can be potentially based upon the diagnostic criteria used by the various groups. The prevalence of DD in one country among different communities or regions may differ considerably (Fig. 4). We have already seen a high prevalence of DD in Bosnia, there is a lower prevalence in the Bosnian Muslim community compared to the Serbian and Croat cohort. Similarly in Norway, after 60 years of age the prevalence of the disease

in the Norwegian community is significantly greater when compared to that of the Sami population. In the UK it appears that a higher reported prevalence is much higher in Scotland when compared to England. Although, again, this may reflect on the use of different diagnostic criteria in different regions (Fig. 4).

Prevalence Rates and its Relation to Assessor of Disease

Of the 49 studies represented in Table 1, not all cases of DD were identified by experienced clinicians. The study by Logan et al. [56] in 2005 identified a high rate of DD in rock climbers; however, diagnosis of DD was made by patients via a questionnaire survey. A high rate of DD identified in the Bosnian community by Zerajic [108] in 2004 may have resulted from the diagnosis of DD made by a junior clinician or non hand surgical specialist. On the contrary, diagnosis made by a medical student or a nurse in a Danish study [36] identified a prevalence rate of 11%. However, this finding may be an underestimate. Diagnosis is likely to be underestimated when it is not made by a

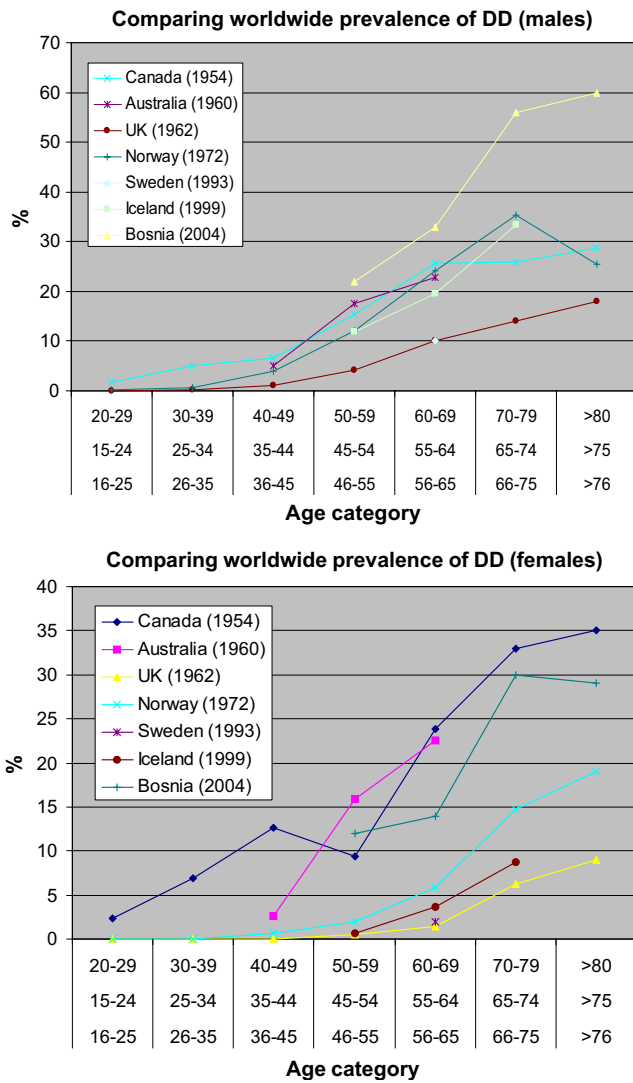


Figure 2 Comparing worldwide prevalence rates in *i* males and *ii* females. The diagnosis of DD in each study was standard with authors having the criteria of identifying nodules, cords, and digit contracture.

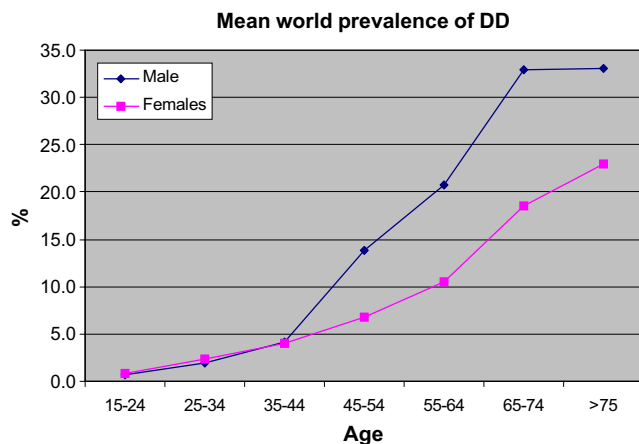


Figure 3 Comparison of prevalence of DD between males and females. Values calculated are mean values from Fig. 2.

specialist hand surgeon. This is highlighted in a study where the prevalence rate of DD was 18% when patients were examined by a physician and 42% when examined by a hand surgeon [78].

Cases of DD in Other Atypical Geographical Locations

As we have seen from Table 1 and Fig. 1, DD appears to be most prevalent in Caucasian males, but not necessarily of Northern European extraction. There are several other reports of cases of DD around the world where one

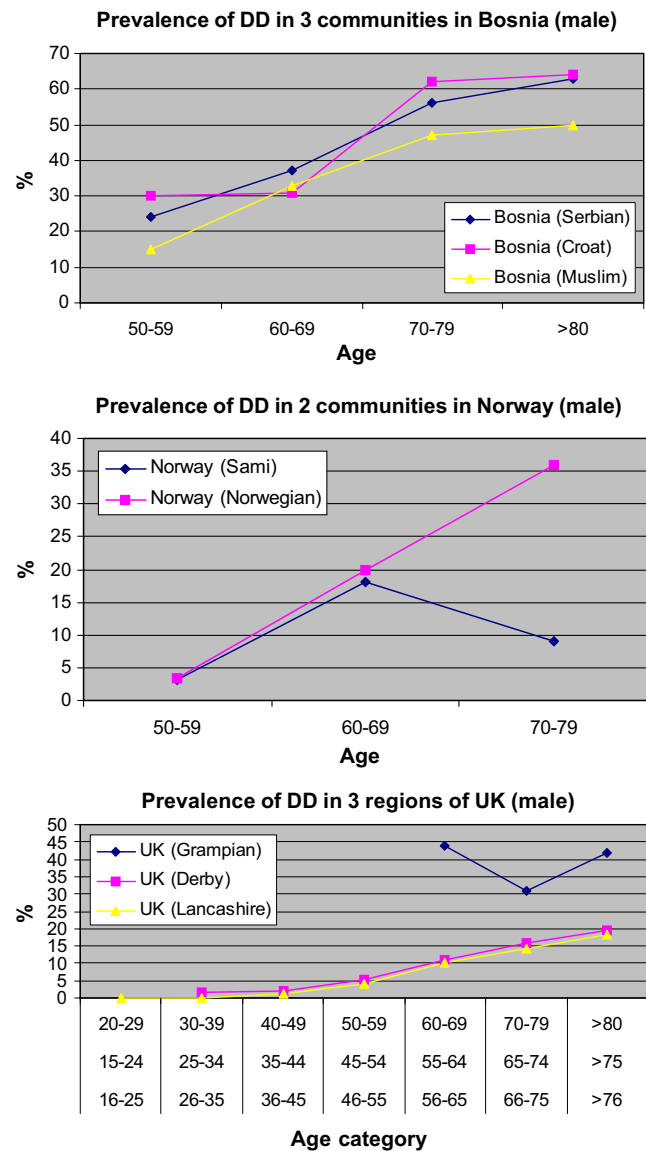


Figure 4 Comparison of prevalence of DD in different communities/regions in *i* Bosnia, *ii* Norway, and *iii* UK. The results in Norway and Bosnia are likely to be real differences in rates of DD as the patients have been examined by one author. However, in the UK, the differences may be as a result of different diagnostic criteria.

would not expect to find the disease [27]. Sladicka, Plasse, and Zaworski identified DD in an African–American patient [85, 94, 106]; these cases were completely sporadic with no evidence of familial clustering or interracial marital relationships. The patient reported by Zaworski in 1979 did, however, have epilepsy and worked as a manual laborer [106].

Similar sporadic cases were identified by Furnas in East Africa in 1979 [34], by Mennen, Richard-Kadio, and Aladin in 1990 and 2001, respectively, in an African patient [2, 70, 90] and by Maes and Pai in 1979 and 1994 in Taiwan [62, 80]. It appears that disease progression and intraoperative findings are similar in African–American and Northern European patients [37]. Muguti in 1993 identified DD in four indigenous Zimbabwean patients [76]. Three cases were male and one female. There was a history of manual trauma in the male patients and a history of epilepsy in the female patient. None of the cases had a family history of DD [76].

Liu in 1991 identified 41 cases of DD in the Oriental patient between 1970 and 1988 with 35 cases undergoing fasciectomy. There was no mention of familial clustering in this case series [55]. A similar case series has been reported by Vathana [102]. Srivasta in 1989 reported a series of ten cases of DD operated on in a UK hospital, with all ten cases being male (age range 45–68 years) originating from the Indian subcontinent [96]. None of the cases had a positive family history, three had recurrent disease, and eight out of ten had a history of repetitive hand trauma. This important publication raises questions of a possible long term environmental factor. Mitra reviewed 23 patients with DD of non-Caucasian origin and commented on these patients having a less extensive degree of DD diathesis [75]; again, in this series of patients, there was no mention of family history.

The majority of the studies reviewed have been those within the English literature. Although this review provides an exhaustive geographical representation of the epidemiology of DD, it may not be complete.

Epidemiology of DD and its Relationship to Age and Gender

We have seen from the population studies conducted over the last half century that DD increases with age (Table 1, Figs. 1 and 2). Interestingly, DD has also been frequently recognized in the younger population [86]. The diagnosis of DD is not a common finding in pediatric practice. Differential diagnosis made in a child who presents with a nodule in the hand, contracture of a digit, or a joint knuckle pad on the dorsum of the hand [64, 81] would include sarcoma of the upper limb [89]. A non-familial, sporadic case of DD has been identified in a

child as young as 6 months old [9] which may suggest a new genetic mutation(s) responsible for disease development.

The majority of studies have found that DD is more prevalent in the male population (Table 1, Fig. 2), with a male to female ratio of approximately 5.9:1 [104]. There appears to be a significantly stronger genetic element of DD in women with familial cases of the disease predominantly in women [44, 66].

Incidence and Prevalence of DD

Two key aspects of DD epidemiology in terms of its incidence and prevalence rates are of interest. Incidence rate is defined as the number of new cases of a disease over a specified time period as a percentage of the population as opposed to the prevalence rate which is the current number of cases of disease at a single point time. This review has shown that most studies that have quoted “incidence” rates were in fact referring to “prevalence” rates. Interestingly, only one study to date has calculated an actual incidence rate of DD [48] which identified an increasing incidence with increasing age.

Comparing Epidemiological Data for DD from Different Sources

Each study has provided evidence for contributing etiological risk factors. However, studies are not standardized making epidemiological comparisons rather difficult. Each study assessed population groups of different age ranges. A problem with the calculation of prevalence rates for DD is the inconsistency in which these studies have been carried out. For example, the low prevalence rate calculated by Geohagan et al. in 2004 [35] may be due to the fact that DD is inappropriately coded within the general practice community resulting in a gross underestimate of the actual prevalence of DD.

One complication of several studies evaluating the epidemiology of DD was the experience of the investigator/s involved in diagnosing the disease in patients. Diagnosis of advanced disease is relatively straightforward with extensive signs of digit contracture and prominent nodules, cords, and palmar pits. However, in patients with minor disease, diagnostic criteria can be difficult to interpret [30]. Diagnosis of DD can be presumed to be relatively straightforward; however, this can lead to misdiagnosis or even over diagnosis of the condition. The highest rate of misdiagnosis of DD is most likely when asking a patient to self-diagnose. Therefore, studies attempting to find the prevalence of DD by questionnaires have to be interpreted with caution, e.g., a study in rock climbers via a patient questionnaire survey [56] had as mild DD (presence of palmar nodules only) is

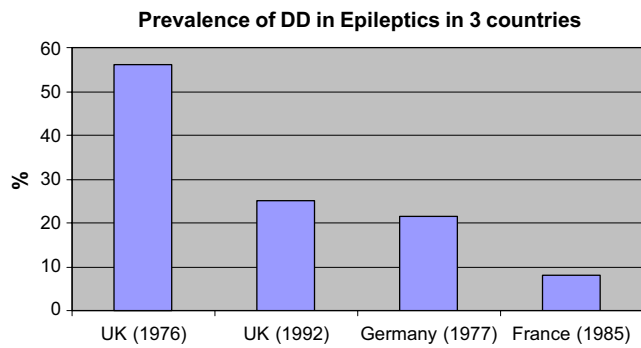


Figure 5 Comparison of prevalence of DD in epileptic communities in three different countries.

likely to be missed, leading to a potentially inaccurate prevalence rate.

Epidemiology Linked to Etiology of DD

Two elements in the etiology of DD clearly continue to stand out. One is the familial nature of the disease and the other is that DD appears to be an extremely common disorder affecting Caucasians of Northern European ancestry [8, 97], although this may reflect the geography of the actual studies. The heritable nature of DD has been of great interest, with reports of the disease present in as many as three generations [84] and studies suggesting a possible autosomal dominant inheritance pattern [67, 84]. There is a possibility that the multi-factorial etiology of DD has a strong environmental factor, based on the results produced by Finsen in 2002 [73] who found that family members were more likely to develop DD if they were residing in the same geographical area as their diseased relative.

The wide variation in prevalence (6–36%) in HIV-infected patients [13, 32] may not be secondary to HIV infection but secondary to the familial nature of DD. Neither study looking at the association between HIV and DD mentioned familial cases in their series of patients. Further studies are required to assess the exact association between DD and HIV.

The origin and spread of DD is presumed to be from Northern Europe [69]. If this is the case, we can see that the DD gene(s) may have spread with its migrating population (Figs. 1, 2). It is surprising that the genetic nature of DD has been discussed for over 50 years; yet, epidemiological studies conducted have not stringently analyzed this aspect of the disease. The presence of sporadic cases of DD around the globe suggests there may be spontaneous genetic mutations causing the disease. The report of ten cases of DD from the Indian subcontinent [96] suggests that environmental factors may also play a role in the development of the disease as all the patients in that series had been living in the UK for several years. DD may not

only be a disease of Northern European Caucasians, the disease in other populations is either not recognized as frequently or there is a lack of initial presentation [63]. This is confirmed with the highest prevalence rates being calculated in Bosnia (males) and Canada (females; Fig. 2).

The presence of DD in children may be secondary to a genetic or environmental influence. The report of DD present in only one identical twin [60] may be the result of sole environmental factors or that the disease may have developed at a later date in the other sibling. Cases of DD in the younger population are likely to have a genetic predisposition, and this should be sought in these patients [50].

Early literature had stated that DD did not occur in women [93]; however, the male to female ratio of DD varies between 7:1 and 15:1 and women tend to suffer more postoperative complications [107]. Females are older at the time of their first operation and have a higher recurrence rate and heritability [44] compared to males [104].

Significance of Associated Risk Factors and Prevalence of DD

Etiological risk factors and their significance have been evaluated by several authors (Table 1, Figs. 5 and 6). The relevance of some of the many implicated etiological factors such as alcohol abuse, cirrhosis of the liver, smoking, epilepsy, diabetes mellitus, and hypercholesterolemia on the prevalence of DD is questioned [17, 57, 92].

Alcohol consumption has doubled over the last 40 years [53]. The prevalence of DD appears to have increased, but estimated rates after 50 years have not doubled, suggesting that alcohol consumption is unlikely to be the direct cause of the disease. The prevalence of smoking is decreasing [83]; there is an unlikely increased risk associated with smoking habits and the development of DD. In spite of this, cigarette smoking and increased alcohol consumption are more likely to result in surgical, rather than conservative management of DD [81]. In relation to smoking, epidemi-

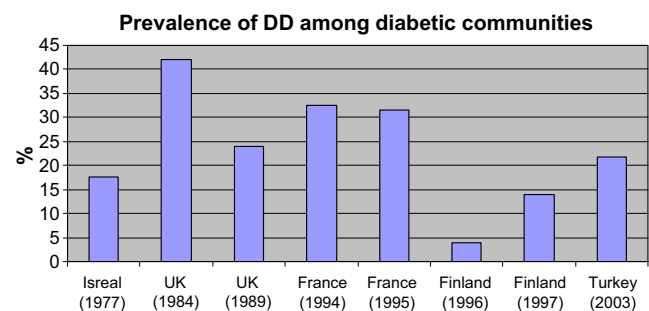


Figure 6 Prevalence rates of DD in diabetic communities. Note that prevalence of DD in study conducted in Finland (1996) examined patients between the ages of 21 and 39 years. Other studies conducted included a wide age range between 30 and >70 years.

ological studies have attempted to identify the risk of mortality, in particular cancer mortality in patients with DD. Gudmundsson concluded that mortality in DD patients is higher [91]. This may be an observational finding and not have any actual significance as DD severity increases with advancing age, as does the incidence of cancer.

Hypercholesterolemia is known to increase with age as does the prevalence of DD, it is also known that patients with DD are more likely to have raised serum triglyceride concentrations [22]; with an aging population both hypercholesterolemia and DD are likely to become more prevalent and hence an increased prevalence of hypercholesterolemia may not be directly related to an increased prevalence of DD.

The prevalence of diabetes mellitus is increasing [46], and there is a positive association with diabetes mellitus and DD (Table 1, Fig. 6). A large retrospective study evaluating the experience of treating DD in one center concluded that there was no significant correlation between DD and diabetes mellitus, alcohol consumption, heavy smoking, or epilepsy; however, the prevalence of these risk factors is greater in DD patients than in the general population [61]. All these factors associated with DD can be debated as to their role in the pathogenesis of the disease; therefore, the change in prevalence rate of DD cannot be confidently attributed to the change in prevalence of these associated factors.

Hand trauma and a history of manual labor are an integral part of establishing whether they are causes of disease development with suggestions that DD is, in certain cases, precipitated or aggravated by hand injury, hand infection, elective hand surgery [1, 58, 72], and vibration exposure [54]. It has gone so far to associate other musculoskeletal conditions with DD which have an increased prevalence in manual workers; a recent study has concluded that patients with a history of frozen shoulder are eight times more likely to develop DD [95]. Since this finding, a further study has concluded that occupational history and social class has no bearing on DD development or progression [48].

A history of rheumatoid arthritis has a negative correlation with DD [4, 39]. There may be a common genetic pathway in the development of carpal tunnel syndrome and DD with chromosomal instability present in the palmar fascia in both of these conditions [11]. It would be important to establish an epidemiological link between carpal tunnel syndrome and DD in order to gain more of an insight into the etiology of both these conditions.

The changes in estimated prevalence of DD may be attributed by an increase in awareness of disease. There have been many reports of sporadic cases of DD in populations we would never expect; again, a full epidemiological study in these populations to calculate the actual prevalence or incidence in these communities has not been carried out. For accurate comparison in different population groups more standardized epidemiological studies need to be conducted.

Conclusion

This review has provided a detailed and thorough account of the epidemiology of DD to date. It gives a concise yet insightful summary of all the studies conducted to date with an attempt to accurately calculate the prevalence and incidence of DD in addition to known etiological factors. The prevalence of DD in different geographical locations is extremely variable, and this maybe due to a genetic element, environmental, or a combination of the two. There have been many prevalence studies which have been informative however the number of true incidence studies is limited. The majority of the prevalence studies have been conducted in Scandinavia or the UK and the vast changes in population structure, changes in prevalence of associated diseases and the change in diagnostic criteria of DD makes further elucidation of the epidemiology of this condition an intriguing challenge.

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