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Rivista di psichiatria 2024; 59: 4-12

Huntington's disease prevalence in Asia: a systematic review and meta-analysis

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Summary. Introduction. The epidemiological studies on Huntington's disease (HD) in the Asian population suggest that prevalence rates are significantly lower than in the Western population. We conducted a systematic review of epidemiological studies of HD in Asia to compare the level of impact of the disease on the Asian population. **Methods.** Original articles and reviews about HD prevalence in the Asian population were found through databases such as Embase, Medline, and PsychInfo. Relevant articles were analysed by scrutinising of references, including specific key words. A meta-analysis was performed on prevalence rates to find the degree of similarities with I2. Point Prevalence was measured as the number of people affected by HD in a 100,000 population and expressed as Point Prevalence (PP)= Number of people affected/100,000 with 95% Confidence Intervals (CI95). **Results.** Results from the random-effect meta-analysis show the highest point prevalence of HD in the Middle East with PP=4.0 (CI95=2.90-5.30). The lowest point prevalence was found in the Chinese population with PP=0.25 (CI95=0.16-0.36). Europe remains at a high prevalence compared to Asian countries with PP=1.00 (CI95=0.82-1.19). The overall prevalence in Asia is PP=0.70 (CI95=0.44-1.0). **Conclusion.** Our study reveals that HD disease affects the population of Asia to a lesser extent than in Europe. The plausible explanation for differences in prevalence is that in some countries, the affected individuals will not self-refer to HD screening for fear of social stigma, negative influence in marriage, and lack of genetic and neurological testing. Another explanation is that studies that used genetic testing exclusively were able to identify the CAG repeats, subgroups of CAG repeat A1 & A2, and haplogroup C, which has less predisposition to high HD prevalence in Asians compared to the Caucasian population.

Key words. Asia, Huntington's disease, meta-analysis, prevalence, systematic review.

Prevalenza della malattia di Huntington in Asia: una revisione sistematica e meta-analisi.

Riassunto. Introduzione. Gli studi epidemiologici sulla malattia di Huntington (HD) suggeriscono che i tassi di prevalenza nella popolazione asiatica sono significativamente inferiori rispetto alla popolazione occidentale. La nostra revisione sistematica ha mirato a stimare la differenza in prevalenza di HD nei paesi asiatici. **Metodi.** Articoli e recensioni originali sulla prevalenza della HD nella popolazione asiatica sono stati trovati attraverso database come Embase, Medline e PsychInfo. Gli articoli rilevanti sono stati analizzati con il vaglio dei riferimenti, comprese le parole chiave specifiche. È stata eseguita una meta-analisi sui tassi di prevalenza per trovare il grado di somiglianza con I2. La prevalenza puntuale è stata misurata come il numero di persone affette da HD su 100.000 abitanti ed è stata espressa come prevalenza puntuale (PP)= numero di persone colpite/100.000 con intervalli di confidenza al 95% (CI95). **Risultati.** I risultati della meta-analisi a effetti casuali mostrano la prevalenza del punto più alto di HD in Medio Oriente con PP=4,0 (CI95=2,90-5,30). La prevalenza del punto più basso è stata trovata nella popolazione cinese con PP=0,25 (CI95=0,16-0,36). L'Europa rimane a una prevalenza elevata rispetto ai paesi asiatici con PP=1,00 (CI95 = 0,82-1,19). La prevalenza complessiva in Asia è PP=0,70 (CI95=0,44-1,0). **Conclusione.** Il nostro studio rivela che la malattia di Huntington colpisce la popolazione asiatica in misura minore rispetto all'Europa, sebbene alcuni paesi come il Medio Oriente presentino la prevalenza maggiore. La spiegazione plausibile per le differenze di prevalenza è che in alcuni paesi gli individui colpiti non si sottopongono allo screening per la HD per paura dello stigma sociale e dell'influenza negativa nel matrimonio e della mancanza di test genetici e neurologici. Un'altra spiegazione è che gli studi che hanno utilizzato i test genetici sono stati in grado di identificare solamente le ripetizioni CAG, sottogruppi di ripetizioni CAG A1 e A2 e anche l'aplogruppo C, che ha una minore predisposizione all'elevata prevalenza di HD nella popolazione asiatica rispetto alla popolazione caucasica.

Parole chiave. Asia, malattia di Huntington, meta-analisi, prevalenza, revisione sistematica.

Introduction

Huntington's disease (HD) is a neurological condition that progresses and has a unique phenotype[1]. Chorea and dystonia, incoordination, cognitive deterioration, dysphoria, agitation, irritability, apathy, anxiety, delusions, and hallucinations are the major neuropsychiatric and behavioral symptoms[2,3]. According to HD estimate, there are more than ten-fold differences across different geographic areas in the

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world[4]. There is presently little published data on research undertaken in Asia. However, numerous studies carried out in Europe, America, and Australia on the incidence and prevalence of HD studies. All of the epidemiological research currently available on the global estimate of HD prevalence point to a greater incidence in European populations than in East Asia, according to preliminary findings[5].

Although HD has a stable prevalence among most white populations of about five or seven affected individuals per 100,000, it has shown a steady increase in prevalence among white people over the last 10-20 years compared to other ethnic groups, and this fact relates to a higher frequency of huntingtin alleles with 28-35 CAG (Cytosine-Adenine-Guanine) repeats in white individuals[5]. However, the overall prevalence in Asia ranges from 0.5 to 1.5 per 100,000 population[5]. A worldwide estimate of HD is 4.1-8.4/100,000 people in the USA[6] with a higher prevalence in the Lake of Maracaibo of 700/100,000[7], Island of Mauritius 46/100,000 and Tasmania 14.4/100,000[8], Europe 1.63-9.95/100,00 with Finland and Japan with less than 1/100,000[4].

Studies conducted before the HD gene was discovered in 1993 may have overestimated the actual incidence by up to 14 per cent globally[9,10]. Small sample numbers and the lack of genetic confirmation in studies done in Africa make it possible for the frequency of HD to be overestimated[11]. A systematic meta-analysis review found that the overall prevalence for non-Asian studies was 5.7 per 100,000, while the overall majority for Asian studies was 0.4 per 100,000 people[4]. The most recent evidence meta-analysis demonstrates a growing HD incidence in the Caucasian population, and studies have called for more HD epidemiology studies in South America, Africa, Central and Eastern Europe, and Asia[5]. It is thought that an increase in prevalence may be mainly attributable to longer lifespans in the population and maybe longer survival times for HD patients as a result of improved treatment[5].

According to research based on diagnoses made in general practitioners' (GP) or family doctors' records, there was an increased in the prevalence of HD in the UK between 1990 and 2010. This increase is attributed to a rise in incidence, improved diagnostic criteria and tests for HD in patients with atypical symptoms, and GPs' increased willingness to diagnose HD in patient records[12]. Other studies in the UK that used the same database and same research period addressed the potential cause for the rise in HD incidence by pointing to improved HD recording by family physicians, a drop in HD stigma, and an improved survival rate[12]. A large majority of new patients do not have a family history of HD, according to several studies in recent years; however, the proportion of late-onset cases (at least 60 years old at start) has grown, as shown by the relatively high incidence of HD in older adults[9-14].

The present study's authors incorporated papers describing molecular processes of diagnosis to account for the differences in epidemiological studies, which would ultimately improve the trustworthiness of epidemiological studies on HD. Though the precise molecular processes underlying the instability of the CAG repeat are unclear, new studies have shown that CAG expansions of the Huntingtin gene are becoming more often linked to a specific chromosome 4 haplogroup A, notably subgroups A1 and A2[15]. In Asian communities with low HD prevalence, these subgroups are not present. Haplogroup C, which has a lower likelihood of growth and maybe different expansion processes than haplogroup A[15], is most often linked to HD in Asian populations. In addition, the frequency of HD is growing in Caucasian populations, reaching 10 per 100,000 or higher[5]. In general, Europeans have a greater HD frequency than East Asian populations[15]. Additionally, it is recommended that genetic testing be included in the investigation of HD prevalence since, in Asian nations compared to European countries, the incidence of concomitant neurodegenerative disorders might mirror HD[16,17].

Epidemiological parameters for the prevalence studies of Huntington's disease

The genetic origin of chorea was recognised in the 19th century, but George Huntington's concise description of the disorder's symptoms led to the disease's eventual naming as Huntington's disease[18]. The mutant protein known as 'Huntingtin' that causes Huntington's disease is produced by an enlarged CAG (Cytosine-Adenine-Guanine) repeat that leads to a polyglutamine band with a variable span at the N-end extension and results in a toxic gain of the role[19]. Although HD may strike at any point between birth and later life, the disorder's typical symptoms appear around the middle ages[19].

Use of brain images in epidemiological studies

In moderate-to-severe Huntington's disease, Stober et al. (cited in Masucci et al.)[20] demonstrated a loss of striatal volume and an enlargement of the frontal horns of the lateral ventricles on regular MRI and CT scans. However, it has been shown that this approach was neither sensitive nor specific[21]. Few functional MRI investigations and PET studies have demonstrated early alterations in afflicted brains before the development of symptoms[2]. As early as 11 before the illness's beginning, some MRI methods may accurately quantify the early detection of alterations in the caudate and putamen regions of the brain[22,23]. Brain MRI reveals structural and functional

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anomalies in the cortical and subcortical areas with loss of striatal volume and increased or decreased activation of the cortical regions in preclinical and clinically visible HD-gene carriers with no evidence of neuropsychological impairment[24,25]. The more recent TRACK HD 12-month longitudinal prospective study using 3T MRI scans showed clear benefits in identifying structural changes in the striatum of both pre-HD and early-HD patients[26].

Genetic screening in epidemiological research

The gene for Huntington's disease (HD) is located on the short arm of chromosome 42, and it is associated with an expanded trinucleotide repeat and normal alleles at this site containing CAG repeats; when CAG repeats reach 41 or more, the disease will become fully penetrant[7,19,27].

According to studies, this impact causes incomplete penetrance when CAG is at 36-40 repetitions; if 35 or less, this image is not linked to the disorder[28]. Harper found that new-onset instances of Huntington's disease with a low family history are caused by the increase of an allele in the borderline or normal range (28-35 CAG repeats), most often on the paternal side[29]. The amount of CAG repeats typically explains 60% of the diversity in age of onset, with the remaining 40% coming from modifying genes and environmental factors[30]. The CAG repeats exhibit instability during replication, which causes both expansion (73%) and contraction (23%); the fluctuation is more pronounced during spermatogenesis than oogenesis; therefore, considerable CAG repeat expansion during replication only occurs in males[29]. Despite a strong initial interest in European surveys[31,32], less than 5% of those at risk for Huntington's disease decide to seek predictive genetic testing. Furthermore, only those over 18 may take the test at a Regional Genetic Clinics in the UK[33]. In addition, prenatal testing and counseling for those who received negative findings are crucial to alleviating concerns regarding HD inheritance[34].

Aim of the study

According to epidemiological research on HD, prevalence rates in the Asian population are much lower than in the western population. According to early findings, HD is underdiagnosed in various Asian nations because of stigma surrounding diagnosis, normalising behaviors, or the lack of accessible (genetic and neurological) techniques for HD diagnosis. To emphasise HD's effects on the Asian population and to compare it to the rest of the globe, this systematic evaluation of epidemiological data on HD prevalence in Asia was conducted. According to the authors' preliminary study, the three Asian regions with the most remarkable occurrence are Pakistan, Punjab, and Gujarat[35]. Forty to One Hundred persons per million in the Western population are thought to have HD (or 0.40 per 100,000)[36].

Methods

Research hypotheses

Null Hypothesis H_o1: there is no significant HD prevalence between Asia Countries.

Null Hypothesis H_o2: there is no difference between the prevalence of HD in Asia and Europe.

Objectives of the search

The primary goal was to measure HD's prevalence in Asia. The prevalence was computed as the proportion of HD patients in a population of 100,000. The secondary objective was to conclude supporting neurogenetic evaluation in HD and mental illnesses generally from the data and literature and reporting on the features of HD evaluation in Asian nations; how various approaches, including neurogenetics, impact HD prevalence estimates was another secondary goal.

Inclusion criteria

Peer reviews were conducted on the publications selected for this systematic review. Some articles had their abstracts translated into English; however, the whole work was not translated due to restrictions on articles and journals. Original primary research, cross-sectional studies, and longitudinal studies, including case reports, were all included in the articles. Since there were no year restrictions, articles published in different years were considered. Until December 2019, all primary studies papers underwent analysis and evaluation (table 1).

Exclusion criteria

Articles that were only available in other languages and were not translated into English could not be utilised. This has reduced the number of available publications. Due to their lack of relevance, articles

Table 1. Number of titles during the Boolean search.

Source	Key words	Number of titles
Embase, Medline, PsychInfo	#1 'Huntington disease'	29,197
	#2 'Epidemiology'	1,640,320
	#3 'Asia'	58,249
	(1 AND 2) AND 3	8

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that provided statistics and information on comorbidities were eliminated. Review articles were left out. Other neurodegenerative diseases, including Parkinson's, Wilson's, Neuroacanthocytosis, and Dentatorubropallidoluysian atrophy, were among the independent morbidities that were eliminated.

Searching method

PRISMA flowchart summarises the selection of articles (figure 1)[36-45]. Access to these databases was established through login to NHS (National Health Service) Athens account. Articles not available on this site were searched through Birmingham University, 'Find it everything', and Google Scholar. The keywords used were *Huntington's Disease* 1), *Epidemiology (as it covers incidence and prevalence)* 2), *Asia, and South-East Asia* 3). The boolean search of titles and abstracts included the terms ("Huntington* AND Epidemiolog*") AND "Asia*"). Search engines included CINAHL, Embase, Medline, PsychInfo, and PubMed. All abstracts and articles with these keywords were analysed, studied and reviewed. Out of the 133 articles emerging from the online database, only four could be selected for qualitative analysis, while only nine studies could be chosen for meta-analysis (tables 1 and 2)[15,38-40,46-54].

The online effect size calculator Lehnard &

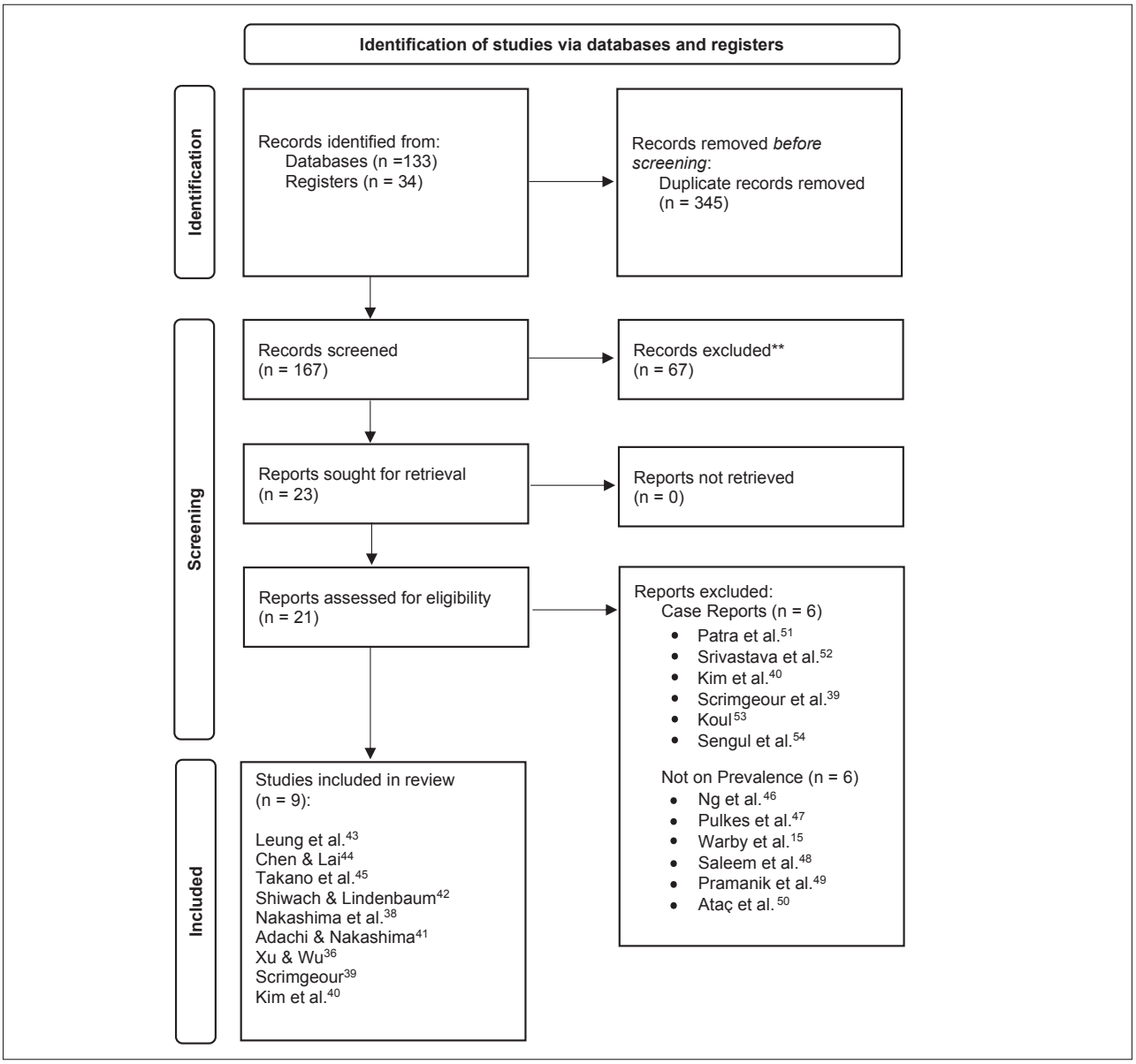

Figure 1. PRISMA Flowchart of relevant literature search.
[From: Page MJ, et al.[37]. For more information, visit: http://www.prisma-statement.org/]

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Table 2. Articles indicated by search engines after selection and exclusion of duplicates.

Sources	Authors
Abstracts of original studies in Japan (the initial studies could not be accessed due to publication in the Japanese language)	Nakashima et al.[38]
Original studies relevant to HD prevalence	Warby et al.[15] Ng et al.[46] Pulkes et al.[47] Saleem et al.[48]
Original reports on the prevalence of HD	Scrimgeour[39] Pramanik et al.[49] Ataç et al.[50]
Case reports on HD	Scrimgeour[39] Kim et al.[40] Patra & Shirolkar[51] Srivastava et al.[52] Koul[53] Sengul et al.[54]

Lehnard[55] and Meta-Excel 5.3 by Epigear International (http://epigear.com/index_files/metaxl.html) have been included in the present investigation. MedCalc® conducted more statistical analyses.

Results

Every study's data were analysed in a meta-analysis to learn more about the point prevalence of HD in population research. The number of afflicted people per 100,000 people is the point prevalence. For each investigation, the authors used Prevalence statistics with 95 per cent confidence intervals (CI95) and the degree of heterogeneity I^2. Funnell's graphic revealed the studies' bias. The meta-analysis results showed an overall PP value of 0.67 (CI95=0.43-1.04), which prevented the Ho1 from being rejected since HD has a negligible effect size (ES) Cohen's d of 0.22. Therefore, the present research confirms that, except for Pakistan, Punjab, and Gujarat, the PP of HD in the Asian Population is low (table 3; figure 2)[36,38-45].

The goodness of fit test calculated the difference between PP in Asia and Europe in the lower and upper limits. The PP in Asia results in 0.67 (CI_{95}=0.43-1.04) × 100,000 vs Europe 1.63-9.95 × 100,000, with no statistical difference between PP_{lower} (p=0.40), and a statistically significant difference between PP_{higher} (p=0.015) hence not allowing to reject Ho2 entirely.

Quality analysis

The Funnel and Doi plots show differences in PP in diverse countries and the possible risk of bias. The coefficient of heterogeneity was statistically significant, rejecting Ho2 for similarities of PP in HD in Asian countries (I^2=94%; p<0.001) (figure 3). Cochrane ROBINS-1 captured the risk of bias in the individual studies[56] being low in all studies (table 4)[36,38-45].

Table 3. Summary of findings of the prevalence of HD in Asia.

Country	Study	Point prevalence	(OR 95% CI)
China and Hong-Kong	Leung et al.[43]	0.25	0.16-0.36
Taiwan	Chen & Lai[44]	0.42	0.30-0.55
Japan	Takano et al.[45]	0.50	0.37-0.64
Pakistan, Punjab and Gujarat	Shiwach & Lindenbaum[42]	1.35	1.14-1.57
San-in area, Western Japan	Nakashima et al.[38]	0.65	0.51-0.81
San-in area, Western Japan	Adachi & Nakashima[41]	0.72	0.57-0.89
Japan	Xu & Wu[36]	0.40	0.26-0.87
Middle East	Scrimgeour[39]	0.40	0.29-0.53
Korea	Kim et al.[40]	0.41	0.30-0.54
Overall prevalence		0.67	0.43-1.04

[a]Point prevalence= number of affected persons × 100,000 inhabitants.

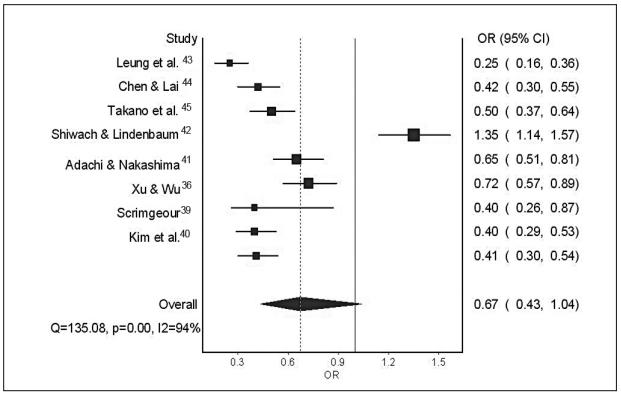

Figure 2. Forest Plot of the prevalence of HD in Asia.

Qualitative critical analysis

Leung et al.[43]: HD disease in China

Reports of HD from 1950-1990 were reviewed. Sixty-nine patients from China and 20 from Hong Kong

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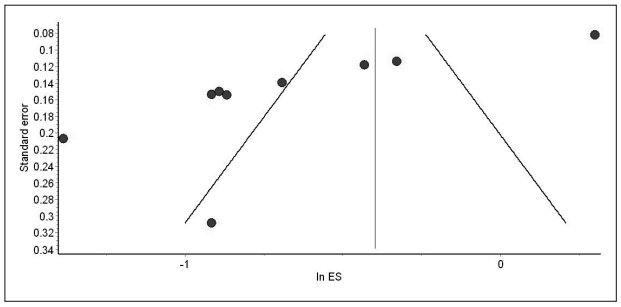

Figure 3. Funnel Plot of risk of bias.

were identified, with a male predominance with an autosomal dominant mode of inheritance. Fifty patients had paternal transmission, and 22 had maternal transmission, which was statistically significant. Sixty-two HD families' ancestral origin was traced, and 73% of 17% of HD patients' families came from coastal and non-costal provenance in China and Hong Kong. This could postulate that HD in the Chinese population might have a European origin.

Table 4. ROBINS-1 template for the assessment of bias in non-randomised studies.

Study	Country	Bias due to confounding	Bias in the selection of participants	Bias in the classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in the measurement of outcomes	Bias in the selection of the reported result	Overall bias
		Is there potential for confounding of the effect of intervention in this study?	Was the selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of the intervention?	Was the information used to define intervention groups recorded at the start of the intervention?	Were there deviations from the intended intervention beyond what would be expected in usual practice?	Were participants excluded due to missing data on other variables needed for the analysis?	Could knowledge of the intervention received have influenced the outcome measure?	Is the reported effect estimate likely to be selected, based on the results, from multiple outcome *measurements* within the outcome domain?	Low / Moderate / Serious / Critical /
Leung et al.[43]	China and Hong-Kong	N	Y	Y	N	PY	N	PY	Low
Chen & Lai[44]	Taiwan	N	Y	Y	N	PY	N	PY	Low
Takano et al.[45]	Japan	N	Y	Y	N	PY	N	PY	Low
Shiwach & Lindenbaum[47]	Pakistan, Punjab and Gujarat	N	Y	Y	N	PY	N	PY	Low
Nakashima et al.[38]	San-in area, Western Japan	N	Y	Y	N	PY	N	PY	Low
Adachi & Nakashima[41]	San-in area, Western Japan	N	Y	Y	N	PY	N	PY	Low
Xu & Wu[36]	Japan	N	Y	Y	N	PY	N	PY	Low
Scrimgeour[39]	Middle East	N	Y	Y	N	PY	N	PY	Low
Kim et al.[40]	Korea	N	Y	Y	N	PY	N	PY	Low

Legend: Y= yes; PY= probably yes; N= no; PN= probably no.

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Chen et al.[44]: HD in Taiwan

This study is Taiwan's first population-based epidemiologic study on Huntington's Disease. A total of 182 cases of HD were identified, including 81 males and 101 females. The overall incidence rate of HD during this period was 0.10 per 100,000 population. The age-specific incidence rates had a peak at 40-49 years in men and 50-59 years in women.

Kim et al.[40]: HD in Korea

The prevalence rate of HD: is based on two data sources, Korean RDR & NHI (National Health Insurance). The total population of Korea in December 2013 was 51,141,463, and the total number of HD cases registered in the RDR database was 208. This study also reviewed patients' CAG repeat length of the normal allele, which was 17.4±3.2, shorter than that of the Caucasian population).

Shiwach & Lindenbaum[42]: HD in Pakistan, Punjab and Gujarat

In 1988, authors identified 17 immigrants (14 families) from the Indian subcontinent affected with Huntington's disease. It was reported that 3 HD patients died in the UK between 1985-1987. One patient committed suicide, and the other had an initial diagnosis of schizophrenia, later confirmed as HD. The above HD patients' crude prevalence rate was estimated at 13.5 cases per million.

Ng et al.[46]: HD in Malaysia: a clinical and genetic study

Seven unrelated patients with HD were identified (4 Chinese, 1 Malay, and 2 Indians) for 18 months. One patient was a native of Malaysia and was the first ethnic Malay with confirmed HD. All patients had more than 35 CAG repeats (range from 40-50) compared to the West population, with a larger mean CAG repeat size. This may explain the high mutation and prevalence of HD in the Western population.

Warby et al.[15]: HTT haplotypes contribute to differences in Huntington's disease prevalence between Europe and East Asia

This study determined the prevalence of Huntington's Disease in Europe and the East Asian population group by analysing the type of HTT (Huntingtin gene) haplogroups. Europeans showed a large CAG repeat size (average 17.8) compared to East Asian populations (16.9). Results showed a more significant part of the Huntington Chromosome in haplotype A among European populations and haplotype C in China and Japan. This study estimated an average prevalence of HD in Europe at 7.5/100.00 population and 10-100 times lower in the East Asia population.

Discussion

According to our research, Asia is less affected by Huntington's disease than Europe. The most extensive worldwide occurrence is seen in various nations, such as Pakistan, Punjab, and Gujarat in India. That certain countries did not implement genetic and neurological testing is a tenable argument. In addition, those afflicted will not self-refer to HD screening because of concern about social shame and a possible impact on marriage. Based on the studies mentioned above, Asia has a low prevalence of HD, with a range of 0.43 to 1.04, which contrasts with the results of a comprehensive review by Rawlins et al.[5], which showed a prevalence of HD range of 0.11-0.725. The lowest HD prevalence in Asia is in China and Hong Kong, which is 0.25 per 100,000 people[4]. Genetic testing for CAG repeats was employed to validate HD's diagnosis in most main studies and additional studies starting in 1993 in East Asian research (Japan, Taiwan, Korea, and China). Other Asian nations, however, did not adopt this strategy. Studies that only relied on genetic testing discovered the CAG repeats, subgroups of CAG repeat A1 and A2, and haplogroup C, which has a lower propensity to high HD prevalence in the Asian population compared to the Caucasian population[15]. Studies from this category included in the present systematic review found this link mainly from Korea, Japan, and Taiwan[38,40,41,46,47,57], and two studies from India[48-50]. The Middle East, and other Asian nations, however, did not experience this[39]. There is no epidemiological research on HD on the Indian subcontinent, despite recent increases in HD awareness and the use of genetic diagnostics. The sole epidemiological study was conducted on Indian immigrants to the UK[42]. There are several case reports on HD prevalence in India, and regional studies are in progress. Still, thorough research on HD prevalence on a wide scale is necessary to consider India's variety and ethnicity and those of neighboring nations on the Indian subcontinent.

There are case reports and individual short reports, but no published verified epidemiological research throughout the Middle East, including Saudi Arabia and Turkey. However, genetic testing has restrictions because of the Middle Eastern population's cultural and religious beliefs[39,53,54]. While most of the first research was conducted in East Asia, including Japan, Taiwan, Korea, and China, the primary weakness of the present study is its sample size. It was challenging to examine early Japanese studies systematically, nevertheless, since many of them were not published in English. The absence of case ascer-

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tainment procedures used in most studies to validate the diagnosis of HD and identify HD individuals is another drawback of the present investigation. Future opportunities exist for this study.

Further study is needed to assess the exact prevalence of HD better since both the Asian and Western populations' total HD prevalence is underestimated. According to studies conducted before the 1993 discovery of the HD gene, the frequency of up to 14% (or 24% globally) may have been overestimated[9,10]. It is important to remember that this is only a supposition and that the actual prevalence is unknown. According to the authors' estimates, the incidence of HD varies by a factor of 10 across different geographic areas of the world[4], which is related to diverse case ascertainment and diagnostic criteria[5]. Other research revealed that the prevalence of HD is associated with various Huntington allele haplotypes with CAG repeats in Caucasian and Asian populations. The rise in prevalence may be partially attributable to population longevity and possibly more prolonged survival of HD patients due to improved treatment[4]. However, this outcome could be an artefact due to more sophisticated and thorough investigations throughout the UK and Europe. This sample size does not accurately represent the incidence of HD in Asia since there are only eight epidemiological studies in Asia, only four of which are accessible in English[40,43,56,57] and four of them are published in Japanese. The actual incidence of HD in Asia is further impacted by the absence of adequate whole-case ascertainment requirements and diagnostic criteria in individual studies/case reports from various regions of Asia. The Middle East has many case reports, but the frequency is overestimated because patients or families of those afflicted refuse the diagnosis, even after getting a second opinion, and refuse pre-test counseling because of cultural and religious beliefs[40]. There are several individual studies[48,49] and case reports[51,52], but no comprehensive epidemiological investigations on the natural frequency of HD in the Indian Subcontinent. The results might be attributed to the stigma associated with HD diagnoses and disapproval of pre-symptomatic HD testing[58].

Conclusions

To further understand HD prevalence and support genetic testing-based diagnostic screening, more study is needed. HD is a fatal illness that destroys the quality of life of patients, their families, and caregivers. Therefore, it is essential to keep giving information, encouragement, and multidisciplinary team care, as well as to carry out research to establish an evidence-based healthcare system for improved HD screening across the board.

Conflict of interest: the authors declare no conflict of interest.

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