The Prevalence of Multiple Sclerosis in the Middle East

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Key Words

Multiple sclerosis, Arabs • Middle East • North Africa • Multiple sclerosis, prevalence

Abstract

Background: The prevalence of multiple sclerosis (MS) in the Middle East has been reported to be low to medium.

Methods: To verify this assertion we conducted a review of published data on the occurrence of MS in the Middle East.

Results: Fourteen studies reporting on the prevalence of MS in the Middle East were initially identified, 5 of which were excluded due to inadequate data or serious methodological limitations. The data from the 9 included studies suggested that the prevalence of MS may vary widely within the Middle East, from low to high. However, these 9 studies were inconsistent in case ascertainment, inclusion criteria and methods of prevalence calculation, and most did not include age/sex standardization. **Conclusion:** Methodological inconsistencies among studies make it difficult to be confident in drawing conclusions about the prevalence of MS in the Middle East. Nevertheless, there is little evidence to support the assertion that the prevalence of MS in the

Middle East is low to medium. Rather, the prevalence of MS in the Middle East may range from low to high, depending on the specific population and environment of study. However, to confirm these findings, further epidemiological research is needed.

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Introduction

Multiple sclerosis (MS) is an inflammatory, demyelinating disease of the central nervous system, which has a progressive clinical course for the majority of individuals. The unique worldwide geographic distribution of MS has motivated many studies as a result of the belief that a better understanding of its epidemiology may yield clues that will help to identify the underlying cause (or causes) of the disease [1]. Kurtzke [2] was one of the earliest researchers to focus on this aspect of MS epidemiology and, based on available studies, he defined high-, medium- and low-frequency bands of MS prevalence. High frequency was $\geq 30/100,000$, medium was $5\text{--}29/100,000$, and low was $<5/100,000$ [3]. Further research confirmed that the frequency bands held true for incidence as well as prevalence, resulting in the widely accepted view that the risk of MS increases with increasing

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Table 1. Excluded studies

Country	Reference	Reason for exclusion
Iraq	6	Reported only the number of cases In-hospital and in-clinic frequency over 10 years, not prevalence, reported
	30	
Jordan	13	No new data reported; refers to data originally reported in al-Din et al. [12]
	14	Reported only the number of cases
	28	No frequency data reported
Morocco	16	No frequency data reported
Saudi Arabia	17	No frequency data reported (letter to the editor)
	18	No frequency data reported (poster abstract)
	25	In-hospital frequency over 10 years, not prevalence, reported
Tunisia	7	Only reported incidence
	21	No frequency data (letter to the editor)
	22	No frequency data (clinical study)
	23	No frequency data (clinical study)

latitude both north and south of the equator. Over time, however, exceptions to the frequency-latitude relationship have been documented [1]. Recent data suggest that racial and ethnic differences within areas may also be important in influencing the worldwide distribution of MS [4, 5].

The role of genetic versus environmental factors in the etiology of MS could be further revealed by studying the Middle East, which has many groups of closely related Arab populations dispersed over a fairly large geographical region. To our knowledge, the frequency of MS in the Middle East has never been thoroughly reviewed.

Here we discuss published data on the prevalence of MS in this region. There are currently too few studies on the incidence of MS to warrant a review at this time. The specific goals of this work are to examine both the quality and quantity of data concerning MS in the Middle East, and to examine these data for possible temporal trends in MS frequency. This research is a starting point for determining the burden of MS in the Middle East and suggesting future research directions.

Methods

Pubmed, Embase and the ISI Web of Science were searched to identify all studies on the epidemiology of MS in the Middle East published to May 2007. Initially, we excluded studies published prior to 1985, the approximate time when magnetic resonance

imaging became part of clinical practice, because MS diagnoses prior to its development are considered to be less reliable. However, due to the scarcity of publications on the epidemiology of MS in the Middle East, we subsequently expanded our time frame to include studies published prior to 1985.

We defined the Middle East as countries in western Asia and northern Africa. Those in western Asia were: Bahrain, Iraq, Israel, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Syria, the United Arab Emirates and Yemen. The northern African countries were: Algeria, Djibouti, Egypt, Libya, Mauritania, Morocco, Somalia, Sudan and Tunisia, and we also included the Comoro Islands. In all 3 databases, we searched for: 'multiple sclerosis' and ('prevalence' or 'incidence' or 'epidemiology') and ('Middle East' or 'Arabs' or each Middle-Eastern country specified above). Including the search term 'incidence' was useful to ensure that prevalence studies misnamed as incidence studies were identified. Additional references were sought from article citations. Although Israel is one of the countries in the Middle East and was included in our initial search, it became clear that studies conducted in Israel were focused on the prevalence of MS in relation to immigration, and they form an important subset of studies that merits a separate review. Thus, for the purposes of this paper, we chose to focus on studies from all Middle-Eastern countries except Israel. Two reviewers (A.B. and J.A.) assessed each study independently. The study methods and results were extracted and tabulated.

Results

Initially, we identified 27 studies on MS in the Middle East that contained epidemiological data as specified in other references, or which we suspected to contain such

Table 2. Studies on MS in the Middle East that reported prevalence

Country	Reference	Study period	Prevalence (per 100,000)	Comments
Iraq	27	1967–1969	3.38 (T)	Kurtzke's approximation used
Jordan	12 26	1992–1993 2004–2005	32.1 (T); 20 (J); 42 (P) 39 (T)	Kurtzke's approximation used
Kuwait	8 9 10 11 19	1983–1984 1988 1980–1989 1990 1991–2000	8.33 (T) ¹ ; 4.44 (K) ¹ ; 7.8 (P) ¹ 9.5 (K); 23.8 (P) 13.3 (T) 14.8 (K); 37.1 (P) 1993: 6.68 (T); 11.02 (K); 3.27 (NK) 2000: 14.77 (T); 31.15 (K); 5.55 (NK)	
Libya	29	1982–1984	5.9 (T) ¹	
Oman	31	1990–2000	4 (T)	Kurtzke's approximation used
Saudi Arabia	15 32	1989 1983–1986	4 (T) 8 (T)	Kurtzke's approximation used
Tunisia	20 24	1985 1974–1978	12 (T) ¹ 3.34 (T)	Inadequate case ascertainment and uncertain at-risk population

T = Total population; J = Jordanian; P = Palestinian; K = Kuwaiti; NK = non-Kuwaiti.
¹ Age- and sex-adjusted to a standard population.

data based on their titles or abstracts [6–32]. After a thorough review of all studies, we found that only 14 contained data relevant to the current study [8–12, 15, 19, 20, 24, 26, 27, 29, 31, 32]. Studies that lacked relevant epidemiological data were excluded [6, 7, 13, 14, 16–18, 21–23, 25, 28, 30]. We noted that 2 of these studies were often incorrectly referenced in other publications as sources of epidemiological data [23, 28] (see below for further discussion of this issue). All excluded studies are listed in table 1. The 14 included studies, which were from Kuwait, Jordan, Saudi Arabia, Oman, Libya, Tunisia and Iraq, are listed in table 2. The included studies used the diagnostic criteria for MS from Poser et al. [33], unless specified otherwise.

Kuwait

Five studies were found on the prevalence of MS in Kuwait [8–11, 19]. The first study was conducted between 1983 and 1984 at the Ibn Sina Hospital (the main center for neurology and neurosurgery in Kuwait), at the Mubarak Al-Kabeer Hospital and at the Al-Emirie Hospital [8]. Eighty-nine individuals (Kuwaitis and residents of Kuwait) with clinically definite MS (CDMS) or laboratory-supported definite MS (LSDMS) were in-

cluded. Of these, 70 were of Arab descent, of whom 27 were Kuwaiti, 25 were Palestinian and the remainder were of various Middle-Eastern descents. The 19 non-Arab MS patients were from several countries. The total prevalence was 6.42/100,000, based on the entire population of Kuwait, while the total prevalence after adjusting age and sex to a standard US population was 8.33/100,000 (4.44/100,000 for Kuwaitis and 7.8/100,000 for Palestinians). The prevalence of MS amongst non-Kuwaitis age- and sex-adjusted to the Kuwaiti population was 7.29/100,000.

The second study was conducted in 1988 at 3 unspecified major government hospitals [9]. Included were 201 individuals with CDMS, LSDMS, clinically probable MS (CPMS) or laboratory-supported probable MS (LSPMS) [33]. Fifty-one were Kuwaiti, 72 were Palestinian, 63 were Arabs from other Middle-Eastern countries and 15 were non-Arabs. The prevalence amongst Kuwaitis was estimated to be 9.5/100,000, based on the total Kuwaiti population on prevalence day. The Palestinian MS prevalence was 23.8/100,000 based on the total Palestinian population in Kuwait on prevalence day.

The third study was conducted between 1980 and 1989 at the Ibn Sina Hospital [10]. It included 194 Arabs with CDMS, LSDMS, CPMS and LSPMS who passed through the hospital's Neuroscience Center during the study period. Their country of origin was not specified. Based on the total Arabic population of Kuwait on prevalence day, the prevalence was estimated to be 13.3/100,000.

The fourth study was conducted in 1990 at the Ibn Sina Hospital [11]. All MS patients known through the Kuwaiti MS registry, which was established in 1980, were identified. Kuwaiti and Palestinian patients who were identified as late as July 1990 were included, as long as their onset was prior to January 1, 1990. The specific classes of MS patients included in the study were not specified. Sixty-seven Kuwaitis who lived in Kuwait between the ages of 5 and 15 years were included in the study. Eighty Palestinians who were born in Kuwait or had moved to the country between 1956 and 1975, and whose symptoms started after arrival, were also included in the study. Using projected population data for 1990 from an official 1975 Kuwait census, the estimated prevalence was determined to be 14.8/100,000 for Kuwaitis and 37.1/100,000 for Palestinians.

The fifth study was conducted between 1991 and 2000 at the Ibn Sina Hospital [19]. Medical files were examined for CDMS and LSDMS patients who were registered at the hospital during the study period. Magnetic resonance imaging was used to confirm MS diagnoses according to the criteria from Paty et al. [34]. The study identified and included 336 patients, of whom 76% were Kuwaiti. The majority of non-Kuwaiti patients were Lebanese. Prevalence, based on census data obtained from the Ministry of Planning and the Civil Information Authority, was reported for each year between 1993 and 2000. Total prevalence was 6.68/100,000 in 1993 and increased to 14.77/100,000 by 2000. Kuwaiti prevalence was 11.02/100,000 in 1993 and increased to 31.15/100,000 by 2000. Non-Kuwaiti prevalence was 3.27/100,000 in 1993 and increased to 5.55/100,000 by 2000.

Jordan

Two studies were found on the prevalence of MS in Jordan [12, 26]. The first was conducted between 1992 and 1993 at the Jordan University Hospital and the King Hussain Medical Center in Amman, the capital of Jordan. Both hospitals are major neurological referral centers for the entire kingdom. The study included 126 Arabic CDMS, LSDMS, CPMS or LSPMS patients who resided in Jordan [12]. The vast majority of non-Jordanians were of Palestinian descent. In this study, the prevalence

was approximated using a method introduced by Kurtzke [35] and Kurtzke and Bui [36] that is designed to estimate MS prevalence in the absence of knowledge of a defined population. The approximation is based on the assumption of a universally constant amyotrophic lateral sclerosis (ALS) prevalence of 5/100,000 and a hypothesized relationship between the number of cases of ALS and the number of cases of MS in a fixed time. The limitations of this technique are discussed later. Using this approximation, the total prevalence of MS in Jordan was 32.1/100,000 (20/100,000 in Jordanians and 42.0/100,000 in Palestinians).

The second study was conducted between 2004 and 2005 at the King Hussain Medical Center and the Al-Bashir Hospital in Amman, and the King Abdullah University Hospital in Irbid, a city in the north of Jordan [26]. The study included 194 individuals who passed through the neurological centers, who were born and still lived in Jordan and who had CDMS or CPMS according to the diagnostic criteria from McDonald et al. [37]. Prevalence was determined to be 39/100,000 in Amman and 38/100,000 in Irbid, based on the respective total number of people served by each hospital.

Saudi Arabia

Two studies were found on the prevalence of MS in Saudi Arabia [15, 32]. The first was conducted between 1983 and 1986 at the King Khalid University Unit, a major neurological referral center in Riyadh, the capital city of Saudi Arabia [32]. Included in the study were 171 native-born Saudis who had CDMS or LSDMS. As in the 1993 Jordanian study [12], Kurtzke's approximation was used to produce a prevalence of 8/100,000.

The second study was conducted in 1989 in the Thugbah community in the Eastern Province of Saudi Arabia [15]. This was a community survey of a variety of neurological disorders including MS, but which primarily focused on seizures, headaches, movement disorders, dementia, stroke and peripheral nerve disorders. Patients were identified in an initial door-to-door screening program conducted by trained interviewers who used a pretested questionnaire administered during a face-to-face interview. Individuals who screened positive for any of the disorders of interest were then evaluated by a neurologist using specific guidelines and defined diagnostic criteria to document neurological diseases. The specific guidelines and criteria used to diagnose MS were not mentioned. All Saudi nationals were included in the study. Only 1 case of MS was identified in the survey of 23,227 individuals, resulting in

an MS prevalence estimate in Thugbah of 4/100,000, based on the total population of Thugbah on prevalence day.

Libya

One study was found on the prevalence of MS in Libya [29]. It was conducted between 1982 and 1984 at the Neurology Unit of the 7th April Hospital in Benghazi, the major neurological referral center for northeast Libya. Additional patients were sought at polyclinics, university hospitals and a center for disabled people. Patients were included in the study if they met the criteria from Schumacher et al. [38] and McAlpine and Matthews [39] for the diagnosis of MS and they had 'definite' or 'probable' MS according to McDonald and Halliday [40]. Of the 29 patients included, 21 were born and spent their childhood and adolescence locally, 5 were referred from other parts of Libya and 3 were from other countries (England, Syria and Pakistan). The ethnicity of the patients was not reported. The estimated prevalence was 4/100,000, based on the Libyan population in Benghazi on prevalence day. The age-adjusted prevalence was 5.9/100,000, as determined by the direct method [41] using the age and sex distribution of the population of southern Hesse, West Germany [42], as the standard.

Oman

One study on the prevalence of MS in Oman was retrieved [31]. It was conducted between 1990 and 2000 at the Sultan Qaboos University Hospital, a major national reference center for neurological studies. It included 30 patients of Omani ethnicity who were newly diagnosed as having MS during the study period. The classes of MS included were not specified. Kurtzke's approximation was used to estimate the prevalence at 4/100,000.

Tunisia

There were 2 studies on the prevalence of MS in Tunisia [20, 24]. The first study [24] was conducted between 1974 and 1978 at the Neurology Center in Tunis, the capital of Tunisia. At the time of the study, it was the only neurology center in Tunisia. Included were 200 MS patients from all over Tunisia who were hospitalized during the study time frame and who fulfilled the diagnostic criteria for MS from McAlpine et al. [43]. However, the author explains that not all MS patients were examined and hospitalized in the Neurology Center, suggesting that the resulting figure is an underestimate. Prevalence was estimated to be 3.34/100,000, based on a total Tunisian population of 6 million.

The second study was a full-scale neurological survey of the residents of Kelibia, Tunisia, in 1985 [20]. A WHO screening tool that had been validated in Nigeria [44] was used to identify individuals with neurological problems. These individuals were then asked to visit a neurologist where their condition could be assessed and a diagnosis could be made if required. In total, 3 cases of MS were identified out of the 34,874 individuals who were screened. However, the neurologists did not use validated, pre-defined clinical criteria for diagnosis and instead relied on clinical and laboratory findings in medical records. The prevalence of MS was estimated to be 9/100,000, based on the total population of Kelibia. The age-adjusted prevalence was 12/100,000 as determined by the direct method [45], using WHO population data (based on data for 46 countries) as the standard.

Iraq

One study was found on the prevalence of MS in Iraq [27]. Records of patients discharged from the department of Neurology at Baghdad Medical Center between 1967 and 1969 were reviewed for MS cases. Eleven MS patients who fulfilled the diagnostic criteria for MS from Schumacher et al. [38] were identified and included in the study. Classes of MS patients included were not specified. Kurtzke's approximation was used to produce a prevalence of 3.38/100,000, although, in contrast to the previous studies, an old estimate of 4/100,000 was used as the ALS prevalence instead of the more recent estimate of 5/100,000.

Discussion

The objective of this research was to examine the quality and quantity of published results on MS in the Middle East. While 27 studies were identified, only 14 were retained for review, of which 5 were judged as providing unreliable information. There was substantial variation in methodological quality and, although some of the included studies might not have been accepted in a more formal systematic review, we chose to include them in our work to provide an *overall* assessment of the published data available at this time.

The mere existence of these studies is a testament to the dedication of the researchers involved, given the often limited medical resources and research infrastructure available in many of these countries at the time the studies were carried out. Nevertheless, the methodological limitations in these studies are problematic and, for the

most part, the results must be viewed with caution. Inconsistencies in case ascertainment, inclusion criteria, methods of prevalence estimation and lack of age/sex standardization were aspects of many of these studies that limit the utility of the results.

In most studies, cases were identified at major neurological referral centers [8–12, 19, 24, 26, 27, 31, 32]. It is reasonable to assume that in Middle-Eastern countries that had few medical institutions most new cases of MS likely passed through the major centers for diagnosis, but the pattern of medical service access and utilization by previously diagnosed MS patients is unknown. Moreover, in some studies [25, 31], cases diagnosed prior to the study period were intentionally excluded. Thus, cumulative incidence, not prevalence, was estimated, rendering a meaningful comparison of results with other prevalence studies impossible. This limitation can be avoided by a systematic search of hospitals, outpatient clinics, individual physicians and MS societies for *all* living MS patients during the study period [46].

Alternatively, community surveys can be used to estimate the prevalence of neurological disorders [44], such as MS [15, 20], in developing countries. A drawback of this method is that it can only be used to estimate prevalence in relatively small areas, because of resource limitations. However, if community surveys are conducted in several areas of the country in a relatively narrow time window, a general prevalence pattern may emerge.

The diagnostic categories of MS (e.g. CDMS or LSDMS) included in the studies also varied. For completeness, we suggest that all classes of definite, probable and possible MS should be included in order to estimate the prevalence of all forms of MS.

The definition of the denominator used to estimate prevalence was not the same in all studies. In some studies the national population was used, but it was not specified whom they included [15, 19, 27, 31]; in other studies, only residents of the country during the time of the study were included [9, 12, 20, 24]. Some investigators tried to determine the 'at-risk' population specifically to use as the denominator. In some studies, the at-risk population was defined as the population of the entire country [8, 9, 11, 24], while in others it was defined as the population they believed was being served by their institution [26, 29]. The definition of the numerator also varied, with some studies including MS patients born and raised in the country [8, 26, 29, 32], while in one study, only those who *resided* in the country between the ages of 5 and 15

were included [11]. Differences in the definitions for the numerator and/or the denominator will clearly result in differences in prevalence estimates, again making comparisons challenging.

Depending upon the selected study design, sometimes the total number of individuals who had MS was not directly obtainable. For this reason, some investigators chose an alternative method to approximate the number of MS cases. Specifically, several authors [12, 27, 31, 32] used a method proposed by Kurtzke [35] and Kurtzke and Bui [36]. This method is based on an hypothesized relationship between the ratio of MS to ALS cases in a particular setting over a fixed time period. Using this approximation, the ratio of MS cases to ALS cases during the same time interval is multiplied by 5 per 100,000, a figure taken to be the standard prevalence for ALS. The use of 5/100,000 for the standard prevalence of ALS is based on the 'quite uniform geographic distribution of ALS (excluding the Marianas and parts of Japan) with a likely prevalence of 5/100,000' [36]. It has since been shown that the distribution of ALS is far from uniform [47]. In fact, ALS prevalence estimates range from 2.3/100,000 in Japan [48] to 6.4/100,000 in central Finland [49]. Furthermore, Kurtzke himself [3] rates studies that have used his approximation method as an 'E' on a scale of comparability that runs from A (best) to E (worst). The use of this approximation is not recommended as there is no evidence that it can be used to reliably estimate the number of cases of MS in a specific time period.

Differences in age and sex structures of populations in different areas made comparison of prevalence estimates from different areas impossible [50]. One way to address this issue is to stratify the study population and compare age-specific prevalence estimates. Alternatively, prevalence estimates can be adjusted to standard populations. In the studies we reviewed, few authors provided age-specific prevalence estimates [9, 11, 19, 26, 29]. Furthermore, even when standardization was carried out, different populations, such as the American, West German and WHO World Standard, were used with no rationale provided [8, 20, 29]. For comparisons to be made between countries and for temporal trends to be identified within countries, age and sex adjustment to a single, standard population is essential.

Taking into account the concerns mentioned above, the validity of MS prevalence figures from 4 studies is likely to be poor owing to the use of Kurtzke's approximation [12, 27, 31, 32]. In addition, results from one other study must be viewed with caution because of inadequate

case ascertainment and uncertainty of the definition of the at-risk population [24].

The available data suggest that the prevalence of MS varies considerably across the Middle East. A low prevalence (4/100,000) was observed in both Saudi Arabia in 1989 and in Libya between 1982 and 1984. A medium prevalence (9/100,000) was observed in Tunisia in 1985, and a high prevalence (39/100,000) was observed in Jordan in 2004 and 2005. MS prevalence in Kuwait increased from 4.44/100,000 in 1983 and 1984 to 31.15/100,000 in 2000. MS prevalence in Palestinians living in Kuwait increased from 7.8/100,000 in 1983 and 1984 to 37.1/100,000 in 1990.

If there has been a true increase in MS prevalence in the Middle East recently, it does not appear to be a unique observation. Similar trends have been observed in Norway [51–53], Mexico [54], Italy [55, 56] and Sardinia [57–60]. However, interpretations must be made with caution as there are many possible explanations for the increase.

It has been shown, for example, that the delay between symptom onset and diagnosis has steadily decreased for MS over the past few decades [61]. Similarly, many milder cases of MS that might have previously gone undiagnosed are now being recognized, thanks to an increased use of magnetic resonance imaging in the diagnosis of MS [62] and superior physician training. Improved medical care for MS patients is also leading to increased longevity [62]. It is also speculated that environmental changes associated with the 1991 Gulf War may have played a role. This idea is based on similar increases in MS prevalence seen in Sardinia and Italy that were shown to be related to the environmental and social changes following the loss of geographic isolation after World War II [4, 57, 60].

Lastly, in our review of the literature, we found 2 instances of inaccurate referencing worth noting. The prevalence of MS in Tunisia in 1975 was sometimes cited as 10/100,000, with reference to a study by Ben Hamida [23]. When we reviewed this study, this estimate did not appear anywhere in the publication. Similarly, the prevalence of MS in Jordan in 1977 has sometimes been cited as 7/100,000, with reference to a study by Kurdi et al. [28]. When we reviewed this study, there was no discussion of prevalence beyond the broad statement that ‘MS is generally believed to be rare amongst Arabs’. Upon further investigation of the literature, we believe that the source of both of these prevalence estimates was a review by Kurtzke published in 1980 [3]. In this review, Kurtzke explains that if all of the definite and probable cases of MS mentioned in the Ben Hamida study [23] came from the cap-

ital Tunis itself, then ‘a prevalence of 10 *might* be inferred’. He also states that, based on the number of MS cases in Jordan observed by Kurdi et al. [28], ‘a prevalence of 7/100,000 might be calculated’. It is possible that this misreferencing of what was thought to be actual results rather than speculative results may have contributed to the misconception that the prevalence in the Middle East is low to medium. This highlights the importance of accurate referencing and the impact that inaccurate referencing can have on an entire field of study.

In conclusion, 14 studies on the frequency of MS in the Middle East were reviewed. The study methodologies were extremely variable, with 5 studies judged to have substantial methodological shortcomings, and which were therefore deemed to be unreliable sources of data. From the remaining studies, the prevalence of MS was found to vary considerably among Middle Eastern countries, from low to high. MS prevalence in Kuwaitis and Palestinians living in Kuwait was found to have increased over the past few decades, from low to high. Whether this variability is the result of the differences in the ways these studies were conducted, limitations in the methodologies, or reflects true differences in the prevalence of MS in the region is a matter for debate and cannot be truly addressed without further studies. To properly investigate this issue, future studies on the prevalence of MS in the Middle East must be carefully designed. Efforts should be made to maximize case ascertainment by searching for MS cases beyond major referral centers. If the research infrastructure does not allow for such a systematic search for MS patients, then community surveys should be considered as an option.

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