Short Communication

An analysis of the prevalence of malaria in Turkey over the last 85 years

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Background: Affecting 106 countries, malaria is a major global burden. Though intensive antimalaria efforts in Turkey have been successful in bringing down the number of cases, historically malaria was a serious public health concern.
Methods: This paper reviews the prevalence rates of malaria in Turkey over the last 85 years (1925–2010). The time series of malaria prevalence was evaluated for possible structural changes by using Chow breakpoint tests and regression models using dummy variables, with autocorrelated errors and generalized autoregressive conditional heteroscedasticity models to assess the impact of volatility in prevalence.
Results: Seventy-eight cases of malaria were diagnosed in Turkey in 2010. Malaria prevalence rates in the country show a statistically significant volatility, which underlines the fragility of efforts to control the disease.
Conclusions: It is necessary to analyse the national malaria control programme to evaluate to what extent its programmatic capacity, financial resources, and political commitment are sufficient to avoid eroding the gains that have already been made and, ultimately, eradicate malaria. It is essential that there should be no lessening in the long-standing efforts to reduce malaria.

Keywords: Malaria prevalence, Malaria control, Burden of malaria, Turkey

Introduction

Approximately half of the world's population is at risk of malaria. According to the World Malaria Report 2010,[1] there were 216 million cases of malaria and an estimated 655 000 deaths in 2010. Mortality rates from malaria have fallen by more than 25% globally since 2000, and by 33% in the World Health Organization (WHO) African Region. Most deaths occur among children living in Africa where a child dies every minute from malaria and the disease accounts for approximately 22% of all childhood deaths.[2]

It is believed that malaria epidemics caused devastation in a number of ancient Anatolian civilizations.[3–5] Although no contemporary data are available, malaria is thought to have been a serious public health concern during the Ottoman Empire, according to accounts in literature and some written documents of that period. Many historians regard malaria and tuberculosis to have been among the main challenges during the Turkish War of Independence (1919–1922).[3–5]

Immediately after the proclamation of the Turkish Republic (1924), programmes were developed to combat malaria. There was strong political commitment to the anti-malaria struggle and the necessary legal, organizational, and financial systems to ensure the effective implementation of the programmes were established. As a result, the number of malaria cases and deaths decreased rapidly.

During the Second World War (1939–1945), however, the number of cases increased (Table 1), mainly due to the disruption in services devoted to combating the disease. There were large outbreaks of malaria both during and after the war. Between 1950 and 1975, the malaria control programme was re-established with government support and malaria was again brought under control (Table 1).

With malaria having been substantially decreased, the budget and level of importance given to the issue were reduced. In the 1970s, health professionals working in the field of malaria control were re-assigned to other areas. At the same time, as these changes were taking place, by the mid-1970s, as a result of DDT resistance and other contextual factors such as the transition to irrigated agriculture, the number of cases had increased to almost epidemic levels (Table 1). In 1977, the official number of patients recorded with malaria reached 115 512. This outbreak was brought under control by the beginning of the 1990s. A second outbreak occurred between

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DOI 10.1179/2047773212Y.0000000064

1993 and 1998. The number of registered cases peaked at 84 345 in 1994 and the outbreak was brought under control by 2000–2001 (Table 1).[3–5]

Since 1926, Turkey has provided diagnosis and treatment of malaria free of charge in the public sector. The main provider of anti-malarial treatment is the Ministry of Health. Transmission is now almost exclusively by *Plasmodium vivax* (*P. vivax*). For treatment of *P. vivax*, 14-day course of primaquine combined with 3-day course of chloroquine is used.[1] In terms of case management, the radical treatment of *P. vivax* cases has been in use since 1926. The gametocidal treatment of *P. falciparum* cases is also in use.[6]

The decreasing trend has continued to the present day with the number of malaria cases having reduced from 9465 in 2000 to 78 in 2010 (Table 1). Of these 78 cases, only nine were documented as occurring among resident Turkish citizens.[6] Regarding malaria risk, Turkey is divided into four main stratums. Stratum I is the endemic area and it includes south-eastern cities. Some provinces in the Stratum I have had indigenous cases since 1974. In 2001, 92% of the reported cases were from this stratum and local transmission is seen mainly in three provinces.

Stratum II includes Mediterranean Sea, Aegean Sea, and Thrace regions and there are respectively limited local or regional epidemics due to imported cases. Stratum II has some indigenous cases time to time. Stratum III is the local epidemics area and it includes central Anatolian cities. Stratum IV (Black Sea and North-east Anatolian regions) is the sporadic area. All malaria cases of Stratums III and IV are imported cases mainly from Stratum I.[4] Malaria surveillance activities have been strengthened all over the country, with priority given to the provinces in south-eastern Anatolia. All foci of malaria are epidemiologically investigated and totally covered

Table 1 Prevalence of malaria in the total population of Turkey during 1925–2010

Year	Number of cases	Prevalence* (‰)	Year	Number of cases	Prevalence* (‰)
1925	1434	1.104	1968	3318	0.988
1926	14 791	11.147	1969	2173	0.631
1927	10 190	7.518	1970	1263	0.358
1928	9928	7.172	1971	2046	0.565
1929	36 186	25.595	1972	2892	0.779
1930	45 653	31.616	1973	2438	0.640
1931	61 241	41.525	1974	2877	0.737
1932	72 500	48.134	1975	9828	2.455
1933	50 609	32.899	1976	37 320	9.121
1934	48 744	31.025	1977	115 512	27.655
1935	40 842	25.453	1978	87 867	20.606
1936	62 466	38.201	1979	29 324	6.736
1937	69 850	41.985	1980	34 154	7.686
1938	81 702	48.270	1981	54 415	11.949
1939	120 060	68.885	1982	62 038	13.288
1940	115 683	65.254	1983	66 681	13.931
1941	94 534	52.659	1984	55 020	11.213
1942	146 077	80.514	1985	47 311	9.404
1943	115 546	63.012	1986	37 899	7.362
1944	80 387	43.377	1987	20 314	3.845
1945	16 739	8.937	1988	16 245	3.050
1946	10 373	5.438	1988	12 112	2.235
1947	5979	3.067	1990	8680	1.575
1948	7298	3.663	1991	12 218	2.180
1949	4973	2.443	1992	18 676	3.277
1950	4211	2.024	1993	47 210	8.152
1951	20 132	9.429	1994	84 345	14.335
1952	8400	3.827	1995	82 096	13.379
1953	5227	2.316	1996	60 884	10.035
1954	2489	1.073	1997	35 456	5.758
1955	1494	0.626	1998	36 842	5.898
1956	1573	0.641	1999	20 963	3.308
1957	5536	2.192	2000	11 432	1.779
1958	11 213	4.316	2001	10 812	1.660
1959	7305	2.733	2002	10 224	1.549
1960	3092	1.124	2003	9222	1.379
1961	3498	1.239	2004	5302	0.783
1962	3594	1.242	2005	2084	0.304
1963	4365	1.472	2006	796	0.115
1964	5081	1.672	2007	358	0.051
1965	4587	1.473	2008	215	0.030
1966	3793	1.188	2009	84	0.012
1967	3975	1.214	2010	78	0.011

Note: *Prevalence per ten thousand.

by indoor residual spraying (IRS).[1] Insecticides currently used in IRS are bendiocarb, pirimiphos methyl, and deltamethrin.[7]

In Turkey, policies and strategies recommended by WHO are implemented for malaria control.

IRS is the primary vector control intervention. Patients of all ages get diagnostic test. Malaria diagnosis is free of charge in the public sector. Also artemisinin-based combination therapies is free of charge for under 5 years old in the public sector. The national malaria strategy aims to eliminate the transmission of malaria by 2012.[6]

Malaria elimination is defined as interrupting local mosquito-borne malaria transmission in a defined geographical area, i.e. zero incidences of locally contracted cases. WHO calls attention to understaffed malaria control programmes as a factor in the failure to eliminate malaria.[8]

Methods

Data on malaria cases were obtained from the Health Statistics of the Ministry of Health.[7,9–16] Province Health Directorates reported malaria cases vertically to the General Directorate of Primary Health Care Services' Department of Malaria Control. Malaria was considered as a notifiable disease in Turkey on 1930, and the data completeness might have been improved after. Throughout the country, there were three malaria control centres in 1924, 11 in 1932, and 16 in 1936–1937 period, respectively. Each centre was divided into 5–10 branches according to the district size and population density. Malaria control activities were covering 54 provinces partially in 1946.[17]

Surveillance activities were carried out by appointed personnel of malaria control departments under the responsibility of province health directorates. As regard to the number of facilities that the data were collected, Table 2 provides information about the district numbers, and mobile service efforts of the 1964–1974 period. Ministry of Health had mentioned that there were missing reportings in the past.[9–11]

The completeness of the data is expected to be similar until 1960s, but improved then year after year. Completeness of reporting, laboratory confirmed cases, and active case detection rates were 100% both in the year 2009 and 2010. On a national scale in 2007, 2008, and 2009, Turkey has reached to the 96% completeness score but the score had been 86% in 2010.[1,6]

The prevalence of malaria was calculated using records of reported malaria cases which were then related to the population census for the respective years. A Chow breakpoint test was used to evaluate any structural changes for the malaria prevalence series for 1928, 1938, 1950, 1975, and 1993.[18] When applying the test, only the intercept model was used. All the time periods, other than 1928, reflected a meaningful structural change (a structural breakdown) at a 5% significance level. Statistically significant differences were found in the trend for the prevalence series but, because there was no explanatory variable, we did not expect useful results or the generation of model assumptions. We, therefore, considered another model where all model assumptions were satisfied.

The second model we used was an autoregressive error model using four dummy variables. We defined the dummy variables as follows:

$$I1 = \begin{cases} 1, & \text{if } 1929 \le \text{Year} \le 1938 \\ 0, & \text{otherwise} \end{cases}.$$

$$I2 = \begin{cases} 1, & \text{if } 1939 \le \text{Year} \le 1944 \\ 0, & \text{otherwise} \end{cases}.$$

$$I3 = \begin{cases} 1, & \text{if } 1976 \le \text{Year} \le 1986 \\ 0, & \text{otherwise} \end{cases}.$$

$$I4 = \begin{cases} 1, & \text{if } 1993 \le \text{Year} \le 1998 \\ 0, & \text{otherwise} \end{cases}.$$

To be able to handle the autocorrelated errors and heteroscedasticity problems, a regression with dummies and autoregressive and an integrated generalized autoregressive conditional heteroscedastic,[19] specifically AR(2)-IGARCH(1,1), error model were used (Fig. 1). After we had considered the distribution of error terms, we decided to use Student's t distributed errors. Thus, all the diagnostics of the model were satisfied. Parameter estimates of the model are given in Table 2. Variables I1–I4 represent the dummy variables. Estimates of first-order autoregression and second-order autoregression are for the autocorrelated error model. ARCH1 and GARCH1 represent the variables of the IGARCH model. TDFI is for the inverse of Student's t distribution with n degrees of freedom. Significance of TDFI parameter from zero indicates differences in estimates under the assumption of normal distribution and under the assumption

Table 2 Parameter estimates of the regression with AR(2)-IGARCH(1,1) error model

Variable	DF	Estimate	Standard error	*t* value	Significance
I1	1	1.7218	0.1704	10.10	<0.0001
I2	1	3.3163	0.4303	7.71	<0.0001
I3	1	0.2316	0.0916	2.53	0.0115
I4	1	0.1893	0.0772	2.45	0.0142
AR1	1	−1.0483	0.0916	−11.44	<0.0001
AR2	1	0.2178	0.0708	3.08	0.0021
ARCH1	1	0.6183	0.0386	16.04	<0.0001
GARCH1	1	0.3817	0.0386	9.90	<0.0001
TDFI	1	0.3252	0.0503	6.46	<0.0001

Note: AR1, first-order autoregression; AR2, second-order autoregression; ARCH, autoregressive conditional heteroskedasticity; GARCH, generalized autoregressive conditional heteroscedasticity; TDFI, inverse of t with degrees of freedom.

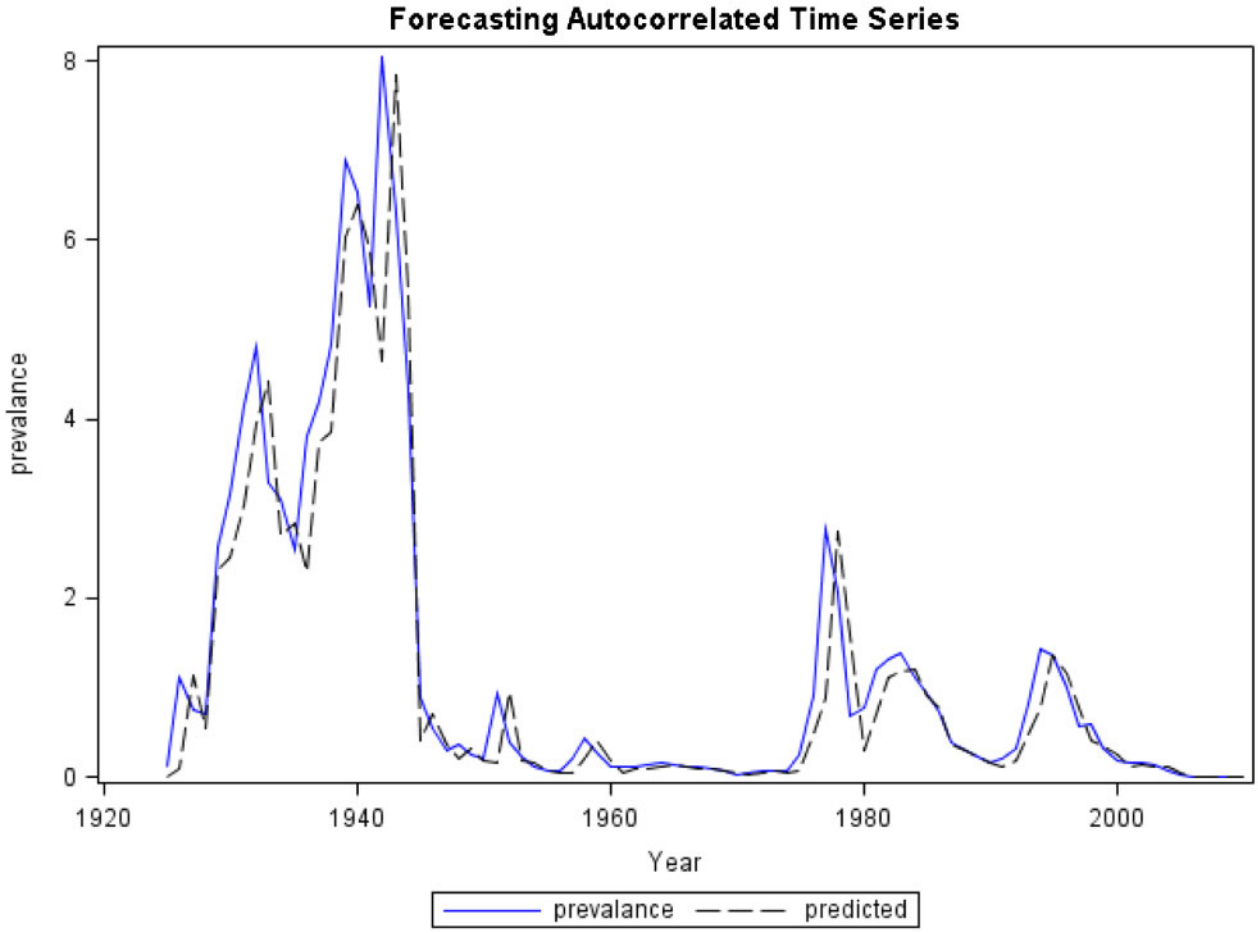

Figure 1 Time series plot of 85 years of malaria prevalence rates in Turkey and the predicted values obtained from the regression with AR(2)-IGARCH(1,1) error model.

of the *t*-distribution. Approximate probabilities given in the last column of the table indicate that all model parameters are statistically significant at the 5% level and they should all be in the model. All dummy variables have an increasing effect on the malaria prevalence series. Table 2 shows that malaria prevalence increases 1.7218 units on average from 1929 to 1938 with the existence of the first dummy variable, and to 3.3163, 0.2316, and 0.1893 units, on average, with the existence of the second, third, and fourth dummy variables, respectively. The coefficient of the determination of the model is 92.13%, which represents a very high percentage in the variation in the prevalence of malaria and is explained by the variation in the given dummy variables. Figure 1 illustrates a close fit to the original and predicted values from the model; this shows the success of the model (Fig. 1).

For the statistical analysis, SAS/ETS® 9.2 (2008) software (SAS Institute Inc., Cary, NC, USA) was used. Here, the time series data were used in the analyses of malaria prevalence. Because of the autocorrelation structure of the series, regular *t*-tests or analysis of variance tests could not be considered for the evaluation of the variation in the behaviour of the series for certain time periods. If either of the tests had been used, the results would not have been reliable because of the theoretical assumptions. The main assumption for the Student's *t*- and F-test is the independence of the series within each group.

Results and Discussion

From the inception of the Turkish Republic, malaria and tuberculosis were its most important health concerns.[5] The pattern of the prevalence of malaria in Turkey in the last 85 years (1925–2010) reflects a statistically significant volatility, which underlines the fragility of malaria control efforts.

As highlighted in the World Malaria Report 2011, the world is witnessing impressive progress in the development and uptake of malaria control tools, resulting in significant reductions in malaria-related morbidity and mortality in many countries.[6,20] On the other hand, each year worldwide, there are up to three million deaths due to malaria and close to five billion episodes of clinical illness, possibly meriting anti-malarial therapy.[21] A stronger and more agile policy setting approach is increasingly important and necessary in the face of a projected shortfall in funding and growing resistance of *Plasmodium falciparum* to anti-malarial drugs and of anopheline mosquitoes to insecticides.[20]

Conclusions

Turkey has a high risk of malaria transmission because of increasing internal and external population mobility. Besides irrigated agriculture, resistances to anti-malarial drugs and to insecticides are some other factors that might affect the pattern of malaria prevalence rates. Malaria was a health concern in the past in Turkey and remains a public health issue today.

WHO advises countries considering malaria elimination to undertake a rigorous scenario planning exercise that considers the epidemiological and entomological situation, programmatic capacity, financial resources, political commitment, and potential threats to success, such as war and mass migration.[8] A current concern for Turkey is whether it has sufficiently robust surveillance systems in place to enable it to not only identify instances of malarial infection from residual sources inside the country, but to also identify new sources of the disease originating from outside the country. Unless these systems are in place, it will not succeed in eliminating malaria.[8] It is important to view malaria elimination as a process of long-term intervention, rather than as a series of rapid, intense actions.[8]

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