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Malaria in Iran: Past and Present Situation

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Abstract

Malaria had being widely prevalent for a long time in Iran. Before starting any anti-malarial campaign in Iran about 60% of population was living in malaria endemic areas. In hyper-endemic areas, approximately 30 to 40% of the total mortality was due to malaria. The malariometric data, reported during 1921-1949 in the malaria surveys in some endemic areas, showed high endemicities of the disease in most parts of the country. The first malaria-training course for preliminary operations of anti-malaria campaign was started in Iran in 1945. Afterwards, in the courses conducted, mostly by the Institute of Malariology many technical personnel were trained. In 1947, for the first time DDT was used in mosquito control in a pilot study in malaria hyper-endemic villages near Tehran. It caused great reduction in malaria transmission. Anti-malarial campaign including drug prophylaxis and treatment, anti-mosquito spraying with DDT and some anti-larval control measures, carried out during 1948-1956, considerably decreased malaria infection rate in most endemic areas. In 1957, malaria eradication programme (MEP) started in Iran and up to 1980 almost interrupted malaria transmission in the north parts of the country. However, in the south parts although the infection rate considerably decreased, but due to some technical and operational problems, malaria transmission was not interrupted. Therefore, in 1980 the MEP shifted to malaria control programme (MCP) which has been continuing up to present time. From 25 species of *Anopheles* found in Iran, 8 species of *A. stephensi, A. fluviatilis, A. culicifacies, A. pulcherimus, A. d'thali, A. superpictus, A. sacharovi* and *A. maculipennis* are considered to be malaria vectors. The prevalent species of *Plasmodia* in Iran are *P. falciparum* and *P. vivax*. *P. malariae* is rare. The main problems, in the malaria endemic areas of the southeast parts of Iran are resistance of the main vectors to some insecticides as well as high resistance of *P. falciparum* to chloroquine. The total reported malaria cases in Iran from 96340 with 45% *P. falciparum* in 1991, gradually, decreased to 18966 with 12% *P. falciparum* in 2005. About 30 to 50% of malaria patients have been among foreign immigrants.

Keywords: *Malaria, Situation, Iran*

Introduction

Malaria had being widely prevalent for a long time in Iran. Avicenna, the Iranian philosopher and physician, (980-1037AD) about 1000 yr ago described the clinical features of an intermittent febrile attack with 4-12 h period of cold, hot, and sweating stages which is actually the characters of paroxysm of malaria (1).

Before starting any anti-malarial campaign in Iran about 60% of 13 millions populations on that time were living in malaria endemic areas and 4 to 5 millions of them had malaria infection each year (2). The first scientific survey of malaria in Iran was started by Latychev in 1921. He studied malaria in Rasht and Bandaranzali in Gilan Province, Caspian littoral areas. In that survey spleen rate was 52.7% and parasite rate was 19.2% with parasite formula (percent of each species of *Plasmodia*) of 56.6% *P. falciparum*, 32.4% *P. vivax*, 4.7% *P. malariae* and 6.3% mixed (3, 4).

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In 1924, Dr. John Gilmour from World Health Organization was invited by Iranian government to study the status of malaria and other infectious diseases in Iran. He found malaria as the most prevalent disease with high morbidity and mortality. As he stated, in one village, 20 km. from Tehran, the spleen rate was as high as 85-100% and the oldest resident was a man 45 yr old (4). Afterwards, some foreign and Iranian investigators in preliminary surveys studied more or less parasitological, entomological and epidemiological aspects of the disease mostly in the Caspian areas in the north and Persian Gulf littoral and plain areas in the south parts of the country where malaria was highly endemic (4, 5-7). In these two regions, about 25% of the patients who were referring to dispensaries had malaria symptoms and approximately 30 to 40% of the total mortality was due to malaria (2, 4-6).

In respect to epidemiological conditions of malaria, Iran had three different regions with various endemicities (6):

i) North region, the littoral plain of Caspian Sea and forest areas of north slops of Alborz Mountains, which has Mediterranean weather with 800-1200 mm. annual rainfall, 70-100% relative humidity, and 10-35 °C, average temperature. The unstable malaria in 3-4 mo transmission seasons with meso- and hyper- ndemicities was prevalent. *A. aclipennis* was malaria vector and the prevalent species of *Plasmodium* was *P. vivax*.

ii) Central plateau region, located between Alborz Mountains in the north and Zagross Mountains in the south. The northwest and west parts of this region are mountainous with temperate weather, 250-400 mm annual rainfall, 25-40% relative humidity, and temperature from several degrees minus zero to maximum 35 °C. Malaria transmission season in the plain and mountainous areas were 3-4 and 2-3 mo, respectively, with hypo-, meso- and hyper-endemicities. The malaria vectors were *A. superpictus, A. maculipennis* and *A. sacharovi* and the prevalent *Plasmodia* were *P.* vivax and *P. falciparum*. *P. malariae* was also existed.

The east parts of central plateau is usually a dry desert areas with annual rainfall of 25-50 mm, temperature 0-40 °C and relative humidity 20-50% Malaria was unstable and varied from hypo- to hyper-endemicities with 3-5 mo transmission season. The vectors in limited areas were *A. maculipennis* and probably *A. culicifacies* as well as *A. multicolor*.

iii) South region is located in the south slope of Zagross Mountains and littoral plains of Persian Gulf and Oman Sea. The weather in this region is warm and in some temperate areas with temperature of 12-50 °C, relative humidity 40-80% and 50-400 mm. annual rainfall. Malaria is semistable with meso- to hyper- endemicities. Transmission seasons are 5-6 mo in mountainous areas and 8-9 mo in littoral areas. The malaria vectors have been *A. stephensi, A. culicifacies, A. fluviatilis, A. superpictus* and *A. d'thali*. The prevalent *Plasmodia* are *P. falciparum* and *P. vivax* and in few cases *P. malariae*. The malaria endemicities in different parts of Iran before applying any effective anti-malaria campaign are shown in Fig. 1.

The malariometric data, i.e. spleen rate, parasite rate and parasite formula which were reported in the malaria surveys in some endemic areas, where no effective anti-malaria campaign was applied, during 1921-1949 (4, 5) are summarized in Table 1.

Malaria vectors: *Anopheles maculipennis* in the first survey of malaria in 1921 was most probably identified as malaria vector in Iran (3). Up to 1956 altogether 19 species of *Anopheles* were recognized in Iran (7). Shahgudian in 1960 provided a checklist

and comprehensive keys to the adults and 4th instar larvae of 20 species of *Anopheles* including three varieties of *A. hyrcanus* (8).

In 1934 General Couloyner, Director of Health Office in Iran appointed Dr. Amidzadeh as Head of Malaria Unit in Pasteur Institute, which it was the first malaria unit for malaria study in Iran. Dr. Amidzadeh studied malaria in the malarious areas in the north parts of Iran and treated malaria patients with quinine free of charge (4).

For preliminary operations of malaria campaign, in 1945, a training course was conducted in Khoramabad by Malaria Control Unit of US Army and 28 physicians and technical personnel from Ministry of Health and Iranian Army attended the course (2).

In 1947, Ministry of Health with collaboration of Near East Foundation applied DDT in a pilot study in malaria hyperendemic villages of Varamin near Tehran. DDT showed high effect in reduction of malaria transmission (2). Then, it was also applied in anti-malarial campaign in Khoramshahr district, Khuzestan Province (9).

In 1949 a four month malaria course was conducted and supported by Health Unit of the Plan and Budget Organization of Iran, 15 physicians, and 100 technical personnel for spraying and other field operations of malaria control were trained (4).

Before 1950, the malaria operations included some chemical, mechanical, and biological control, which usually were carried out as pilot studies in some areas (10). Gambusia fish was applied as anti-larval in control of mosquitoes in malaria endemic areas in north parts of Iran by Dr. Amidzadeh (2).

In 1952, Institute of Malariology was established in the Department of Parasitology of the School of Medicine in Tehran University and supported by the Ministry of Health and the Plan and Budget Organization of Iran. The Institute had Divisions of Protozoology, Entomology, Epidemiology, Insecticides chemistry and Statistics for training of technical personnel for malaria control. Moreover, Institute was involved in malaria research programmes and studying malaria situation all over the country. From 1952 to 1956 in 44 training courses 1142 individuals were trained in the Institute as malariologists, epidemiologists, entomologists, microscopists, field malaria surveillance and entomology control agents (2, 4, 11).

During 1952-1955, in malaria surveys carried out by the Institute of Malariology in some malaria endemic areas in Iran, from 5720 villages 312725 individuals were examined and 278440 blood samples were taken. In microscopical examination, 2417 cases (0.87%) were positive: *P. falciparum* 38%, *P. vivax* 49%, *P. malariae* 12.5% and mixed 0.5% (4).

From 1953 to 1956, the Health Collaborating Organization was established in Tehran and anti-malarial units were developed in other provinces. During this stage, about 410, 000 villages with 12, 400, 000 populations were sprayed with DDT.

Anti-malarial campaign including drug prophylaxis and treatment, anti-mosquito spraying with DDT and some anti-larval control measures, carried out in Iran during 1948-1956, considerably decreased malaria infection rate and reduced spleen rate, in malaria endemic areas from 66.9% to 5.2% in the north and the north-west parts of the country, respectively (9, 10).

In 1956, an agreement was conducted for malaria eradication programme (MEP) among Iranian government, World Health Organization and UNICEF. In this programme, Institute of Malariology and Parasitology was involved in malaria training and research activities. Malaria Eradication Organization (MEO) was established

with Divisions of Medical Operation, Field Operation and Administration. MEO was financially supported by Ministry of Health. Some materials and equipments provided by UNICEF. Training of senior technical personnel in international malaria training centers as well as sending malaria advisors to Iran was supported by WHO (2,11).

In preparatory phase of MEP, started in 1957, development of existing information on malaria epidemiology and entomology, providing the essential equipments and materials and training more technical personnel were performed.

The attack phase of MEP carried out in the north parts of Iran with population of 17 millions, more or less interrupted malaria transmission and actually pushed these parts of the country to consolidation phase of MEP in 1968. During 1968-1971 in the south parts of the country with population of 4.072 millions, as anti-malaria campaign with limited spraying, case finding and chemotherapy could not prevent outbreak of the disease, in spite of operational and technical problems existed in this part of the country, the attack phase of MEP was carrying out. In this programme, Malathion was applied in areas where *A. stephensi* was resistant to DDT and Dieldrin. Larviciding using chemical (oiling or Abate) and biological (Gambusia fish) were also used. Malaria case finding and treatment of malaria positive cases with chloroquine and primaquine were carrying out. In areas where the number of malaria positive cases was high, mass drug treatment was also performed. These operations caused 30-90% reduction in parasite rate. But in those areas where in addition to *A. stephensi* other malaria vectors were existed the reduction of parasite rate was not satisfactory (12).

The results of anti-malaria campaign and MEP up to 1973 caused almost elimination of malaria in the north parts of Zagross Mountains, which were in the consolidation phase of MEP. In south parts of Zagross Mountains the incidence of malaria cases considerably reduced and the total annual malaria cases in Iran were coming down to 12000 in 1973. However, these temporary relative successful results of MEP in Iran encouraged the health authorities to integrate MEO in Communicable Diseases Control (CDC). This integration caused reduction of MEP activities and resulted elevation of malaria incidence. Therefore, in 1977 MEO obtained again its autonomy, started more activities, and strengthened its human power for more scientific approach to malaria control, using new larvicides and insecticides for the control of malaria vector in the south parts of Iran that was still in attack phase of MEP. The objectives of anti-malaria campaign were decreasing of malaria transmission and infection rates in the residual foci in south part of Iran and sustaining the north parts free of malaria as far as possible. In fact, these were the objectives of malaria control programme (MCP). Therefore, in 1980 the Ministry of Health according to suggestions of Malaria National Scientific Committee and WHO malaria advisors changed MEP to MCP, which has been carrying out by trained technical personnel of the Universities of Medical Sciences and Health Services in all provinces of Iran. For MCP, existing resources, primary health system and developed health houses were applied for management of malaria as a disease and to take action for case finding, diagnosis, treatment of uncomplicated cases by health workers (Behvars) in health houses and referring the complicated cases to more developed health centers or infectious wards in the local hospitals (13, 14).

MEO in all provinces of Iran is under supervisions of Malaria Division of Dis-

eases Management Center, Health Undersecretary, Ministry of Health and Medical Education. School of Public Health and Institute of Public Health Research, Tehran University of Medical Sciences and Health Services and some other research centers such as Pasteur Institute of Iran collaborate in MCP in scientific advisory and research programmes.

Since 1980, MCP is carrying out in Iran. Now the most important malaria transmission areas i.e. the problem areas are in southeast part of the country including Sistan-Baluchestan, Hormozgan Provinces, and south part of Kerman Province. The present problems of MEP in the south parts of Iran include: plurality of malaria vectors and their various behaviors, resistance of the main vector *A. stephensi* to some insecticides, long distances between some villages without suitable transportation roads, structure of living houses, socio-economic conditions, immigration from malarious neighbors countries and some other operational problems (12, 15).

During the recent years outbreak of *vivax* malaria appeared in the northwest parts of Iran in Parsabad, Ardebil Province (16). The disease in these areas is usually under contol.

The trend of the total malaria cases reported annually by Malaria Unit, Diseases Management, Ministry of Health and Medical Education during 1991-2005 is shown in Fig. 2. In the year 2003, altogether 1353260 blood smears have been micro-scopically examined and 23562 cases were parasitologically positive (16). Annual parasite incidence (API) was 0.35/ 1000 and 19% of malaria positive cases were *P. falciparum*, 80% *P. vivax* and 1% mixed (16). The malaria problem areas were Sistan-Baluchestan, Hormozgan, and some areas of Kerman and Fars Provinces where 90% of malaria cases were reported. Sixty five percent of positive cases were from Sistan-Baluchestan Province. In the year 2002, the total number of malaria cases were 15378 and it was considerably less than the year 2001 (19274 cases) and much less than the year 2003 (23562 cases). In 2002, 52% of malaria cases were among foreign, mostly Afghan immigrants who already had malaria infection as imported cases or some of them might get malaria infection when they were living in malaria endemic areas in Iran (16).

One of the main problems in the control of malaria is resistance of *P. falciparum* to chloroquine and some other antimalarial drugs, which is now more or less common in the malaria endemic areas in the world (17).

In Iran, in two preliminary *in-vivo* studies of the response of *P. falciparum* to chloroquine, carried out in the malarious arias in south parts of the country, during 1968-1976, *P. falciparum* was sensitive to chloroquine (18, 19).

From 1983, the *in-vivo* and *in-vitro* studies of the response of *P. falciparum* to chloroquine and some other antimalarial drugs started in the malarious areas in southeast parts of Iran.

In Iran-Shahr district, Sistan-Baluchestan Province a few chloroquine-resistant cases were found in the *in vivo* test in 1983 and the rate of resistance was 5.7% at RI level (20). The resistance, gradually, increased to 51.2% at RI, RII and RIII levels up to 1996 in this district (21).

In Bandar-Abass and Kahnoudj districts, Hormozgan and Kerman Provinces, the rate of chloroquine-resistant *P. falciparum* cases was 32.5% at RI and RII in 1986-1987, increased to 64.8% at RI, RII and RIII levels in 1994-1996, and was altering between 68% and 84% at RI and RII levels during 1997-2001 (21-23).

In 88 chloroquine-resistant malaria patients who were treated with standard doses

of sulfadoxine-pyrimethmine (fansidar) alone or in combination with amodiaquine and examined by the 28 d *in-vivo* test, in 13.6% resistance were observed at RI and RII levels (24).

In micro *in vitro* tests, using WHO standard kits, the rates of resistance to chloroquine, amodiaquine, sulfadoxine-pyrimethamine, mefloquine and quinine were 33.4%, 15.2%, 17.9%, 2.2% and 0.0% in 281, 72, 39, 44 and 72 blood samples taken from *falciparum* malaria patients, respectively (21).

In a recent study of the *in-vivo* response of *P. falciparyum* to chloroquine carried out in the malaria endemic areas in southeast parts of Iran the treatment failure by the day 28 was 78.5% and only 21.5% showed adequate clinical and parasitological response to chloroquine (25).

The *in vivo* response of *P. vivax* to chloroquine was also studied in 827 malaria patients from the malarious endemic areas in southeast parts of Iran during 1995-2001. The mean of parasite clearance time (MPCT) was 2.78 d and no resistance case was found (26).

Fig. 1: Malaria endemicities in different parts of Iran before applying any effective anti-malaria campaign, 1949

Table 1: Spleen rate, parasite rate and parasite formula in the malaria surveys carried out in some malarious areas of Iran, before applying any effective anti malaria campaign, during 1921-1949

Region	District	Year	Spleen rate	Parasite rate	% Pf	% Pv	% Pm
	Rasht	1921	52	19	44	42	6
	Bandaranzali	1921	53	19.5	69	22	4
North	Tonekabon	1935	64	21	70	13	15
	Chalus	1949	89	31	76	24	0
	Gorgan	1935	31	7	10	64	26
South	Boushsehr	1936	35	18	65	27	8
	Varamin	1940	61	36	100	0	0
Central	Arak	1934	30	16	44	31	19
East	-	-	-	-	-	-	-
Southwest	Behbahan	1934	65	30	80	9	11
	Khoramshahr	1936	43	16	54	40	6

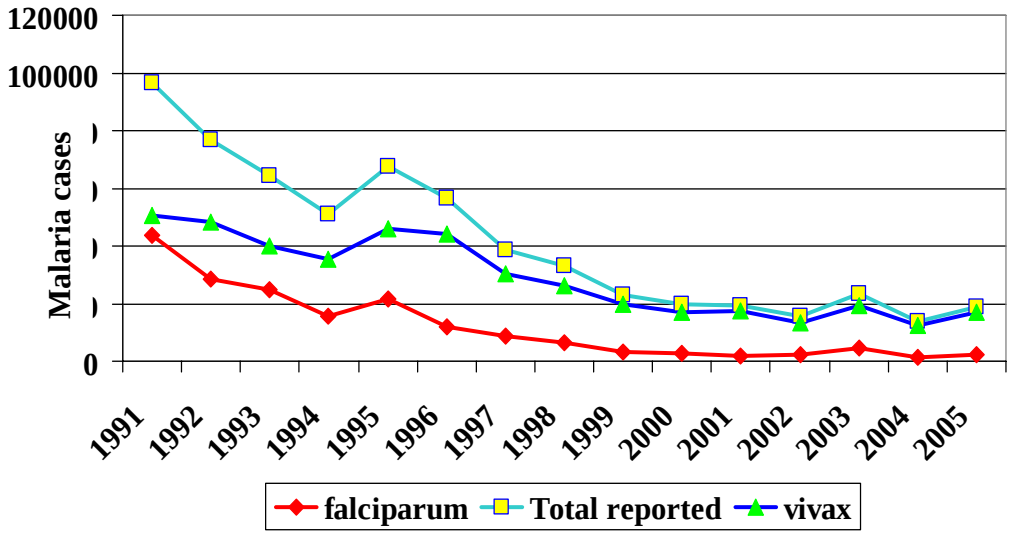

Fig. 2: Trend of the total annual cases of malaria in Iran during 1991-2006, reported by Malaria Division, Disease Management Center, Ministry of Health and Medical Education

Discussion and conclusion

At the end of 2004, 107 countries and territories with about 3.2 billion population lived in areas at risk of malaria transmission. Iran is among the countries located in the Eastern Mediterranean Region with low malaria endemicity and in its some areas, there is the risk of malaria transmission (27, 28). However, 50 to 60 yr ago in most parts of the country malaria was prevalent at hypo- to hyper-endemicities (6). Sixty percent of populations were living in malaria endemic areas. In the highly endemic areas in the littoral Caspian Sea in the north and Persian Gulf and Oman

Sea in the south, 30 to 40% of total mortality was due to malaria (2, 4).

The conditions of geographical, climatic, irrigation, invironmental, tribal and population movement, structure of living houses, transportation roads, and distance among villages, illiteracy, economic and social problems, etc were favorable for malaria transmission and high prevalence of the disease in Iran (10). Before 1950, no effective campaign was applied against malaria in Iran. From 1950 when DDT applied for the control of mosquitoes in malaria endemic areas with some other antimalarial measures such as larviciding, chemoprophilaxis and chemotherapy caused highly decrease in the prevalence of the disease in most malaria endemic areas, particularly in the half north parts of Iran. In the south parts of the country, although the number of malaria cases considerably decreased, but due to some technical and operational problems such as plurality of species of the *Anopheles* vectors, appearance of resistance of the main vector *A. stephensi* to DDT in 1957, then to Dieldrin in 1959 and to Malathion in 1977 as well as the resistance of other vectors: *A. culicifacies, A. sacharovi* and *A. d'thali* to DDT (29- 32) and their behaviors, the efforts for interruption of malaria transmission were not successful. Other insecticides such as Prpocsur, Icon, Actelic and Deltamethrine have been used in spraying for mosquito control in the malarious areas of south-east parts of Iran (Dr. H. Ladoni, personal communication).

However, up to 1979, MEP had caused almost elimination of malaria in the north parts of the Zagross Mountains and considerably reduced the malaria cases in the south parts of the Zagross. Annual parasite incidence (API) which was totally about 350/ 1000 before applying any effective anti-malarial campaign in Iran, highly decreased to 2.14/ 1000 and 0.03/1000, in the areas under the attack and consolidation phases of MEP, respectively, in 1979 (33). However, MEP in Iran during 1957-1979 due to technical and operational problems and existing malaria in some neighbor countries could not interrupt the transmission of the disease all over the country. Therefore, in 1980, the MEP changed to malaria control programme (MCP) which has been continuing up to now.

Up to 1960, 20 species of *Anopheles* were identified in Iran (8). Recently a checklist of 24 species and one new species, *Anopheles peditaeniatus* has been reported (34, 35). Among 25 species of *Anopheles* identified in Iran, 8 species including: *A. maculipennis, A. sacharovi, A. superpictus, A. fluviatilis, A. stephensi, A. culicifacies, A. d'thali* and recently *A. pulcherimus* are considered to be malaria vectors (6, 7, 36-39).

The microplate method of enzyme-linked immunosorbent assay (ELISA), using anti-human alkaline phosphatase conjugate was applied for the first time in 1982 in Iran to identification of *Anophles* mosquito bloodmeals (40).

As human blood index (HBI) is the main factor in vectorial capacity of *Anopheles* mosquitoes, the ELISA was used in 1985 in determination of HBI in 5,325 engorged mosquitoes belonging to 12 *Anopheles* spp. collected from 19 provinces all over the country. The human blood index (HBI) varied from 3.6 to 23.7%. The maximum HBI found in *A. multicolor,* which was previously considered as suspected malaria vector in Iran (6). The HBIs in *Anopheles* malaria vectors of Iran were 12.2, 4.9, 11.4, 9.9, 12.5, 5.1, 3.6 and 4.7 percents in *A. sacharovi, A. maculipennis, A. superpictus, A. pulcherimus, A. d'thali, A. fluviatilis, A. stephensi* and *A. culicifacies* (41).

The prevalent species of *Plasmodia* are *P. vivax* and *P. falciparum* in Iran. The rate of *P. falciparum* during 1991-2005 ranged from 7% to 45% (Fig. 2).

Whenever, the number of total malaria cases were high the rates of *P. falciparum* were also high. The rate of mixed cases in the usual microscopical examination of the Giemsa stained thick blood smears in the malaria endemic areas in the southeast parts of Iran is usually 1 to 2%. However, using molecular PCR technique the rate of mixed cases has been reported quite higher (42).

Rapid immunochromatography test " ICT MALARIA Pf " has been evaluated in diagnosis of *P. falciparum* and it was applied also in parasite detection in the blood of falciparum treated malaria patients who were under 28 d *in vivo* test for assessment of the response of the parasite to chloroquine. The results showed that the rapid test of "ICT MALARIA Pf" is quite sensitive and specific for detection of asexual blood forms of *P. falciparum*. It was also sensitive for detection of scanty number of the parasite in the blood of treated malaria patients, on the day 7 to day 14 after treatment, while the parasite was not found in the related Giemsa stained thick blood films against 2000 white blood cells (43).

After reduction of mosquito transmission of malaria in the malaria endemic areas in Iran, 233 cases of transfusion-induced malaria were reported by Malaria Eradication Organization during 1973-1983. The *Plasmodia* spp. diagnosed in the blood of recipient patients were 78% *P. malariae* and 22% *P. vivax*. On that time, the sources of human blood for transfusion in Iran were the blood of professional donors, which among them some individuals were serologically positive for malaria antibodies and in few cases, scanty malaria parasites were found in their blood samples by parasite concentration technique. But now as the necessary blood units are taken from healthy volunteers donors, the blood induced malaria are found rarely in Iran, usually in the areas where malaria transmission is still occurs (44, 45).

Serological and parasitological surveys of malaria, applying indirect fluorescent antibody technique (IFAT) with *P. falciparum* and *P. vivax* antigens as well as microscopy examinations of the usual and concentrated Giemsa stained thick blood films carried out in malarious areas in south-eastern parts in 1972 and in the north, north west and south-west parts of the country during 1975-1982. The obtained data showed period prevalence of the diseases, in different areas with various malaria statuses. In these studies, more asymptomatic low parasite positive cases were found in concentrated blood smears among sero-positive cases (46, 47).

Resistance of *P. falciparum* to chloroquine has been reported in the world in most malaria endemic areas where the transmission of this parasite is prevalent (17).

In Iran in 1984 five imported cases of *P. falciparum* resistant to chloroquine, including: two Iranian men returned from India and two Afghan and one Bengalee immigrants came to Iran through Pakistan were studied by *in vivo* test and in four of them the resistance was also confirmed by macro *in vitro* test (48). In other studies carried out in the malarious areas of southeast parts of Iran (20- 23) a considerable number of *P. falciparum* chloroquine-resistant cases were among imported Afghan and Pakistani malaria patients. Therefore, the origin of resistant strains of *P. falciparum* in Iran has been most probably, from Southeast Asia (49).

In 2002, 52% and in 2003, 30% of the total malaria cases reported in all over the country were foreign malaria patients which considerable number of them were imported cases mostly from Afghanistan (50).

Now one of the main problems in the control of malaria in Iran is high resistance of *P. falciparum* to chloroquine.

As no significant changes was found in the high resistance status of *P. falciparum* to chloroquine which had being used in the studied areas, therefore, the national policy of chemotherapy of *P. falciparum* with chloroquine alone, changed to combination of chloroquine and sulfadoxine-pyrimethamine (fansidar) or in some special cases artesonate plus fansidar. Although the low resistance of *P. falciparum* to sulfadoxine-pyrimethamine (fansidar) has been also reported (24, 51), nevertheless, fansidar in combination with chloroquine or in some special cases with artesonate has been recommended to be used in treatment of uncomplicated falciparum malaria (52).

As resistance of *P. vivax* to chloroquine has been reported in some malarious areas mostly from South East Asia in Indonesia, Myanmar, Papua New Guina and Vaneato (53), monitoring of the *in vivo* assessment of the response of this parasite to chloroquine in 827 vivax malaria patients in the malarious areas of south-east parts of Iran, carried out during 1994-2001. In these studies, no chloroquine-resistant case was found and the mean of parasite clearance times from 1 to 6 d was 2.87 d (26).

According to the National Strategy Plan for Malaria Control, in respect to malaria status the total country has been classified in four strata (50):

i) Areas where local transmission of malaria occurs such as areas in Sistan-Baluchestan, Hormozgan and south parts of Kerman Provinces and occasionally some areas in Ardebil, Boushehr, Fars and Mashad Provinces.

ii) Areas where the imported cases are found and the potential risk of malaria transmission exists such as areas in Gilan, Mazandaran, and Golestan Provinces.

iii) Areas where the imported cases are found, but there is no risk of malaria transmission such as Yazd, Kurdestan, and Hamadan Provinces.

iv) Areas where no malaria case was reported during the last three years. It seems there was no such area in Iran.

The main technical elements of the strategy of malaria control which are or should be applied in MCP all over the country, particularly in areas where there are local malaria transmissions or there is potential risk of malaria transmission are usually:

i) Early case detection and prompt treatment;

ii) Plan and implement suitable preventive measures including vector control;

iii) Improving information and reporting system;

iv) Providence and prevention of local malaria outbreak or epidemy;

v) Carry on training and refreshing courses for senior staff and technical personnel;

vi) Establish continuous quality control system for malaria microscopic diagnosis and cross checking of examined slides;

vii) Monitoring of the response of *P. falciparum* and *P. vivax* to anti-malarial drugs;

viii) Planning and performing basic and applied researches on the local existing malaria problems;

ix) Sustainous supervision and evaluation malaria control activities;

All of the above activities need financial and scientific support and supervision of the national health authorities and collaboration of academic and research centers as well as the international organizations such as Roll Back Malaria/ WHO (27, 54).

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