MALARIA TREATMENT VS. MALARIA PROPHYLAXIS : A COST COMPARISON.

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ABSTRACT

Aim This research aims to evaluate the cost of using drugs to combat an established infection as compared with drugs used for prophylactic purposes. And this aim was achieved by using the following objective which was: (i) To estimate the cost of using anti-malarial drugs as treatment compared to using them as prophylaxis.

Methods The study used 142 subjects (*n*=142) who had travelled to Liberia for six months to work among the Jordanian Level III Hospital within the United Nations Mission in Liberia (UNMIL). This is a malarious area, so the participants have to take prophylactic medicine, or they will be at risk of acquiring malaria. The prophylactic medicines that have been taken by the participants cost the RMS a particular value (Cost 1), In contrast those who acquired malaria will need treatment and hospitalization and this will incur on the RMS another different set of costs (Cost 2). A questionnaire was distributed among the participants to collect the data needed. In addition, data was collected from the records of the financial offices in the hospitals of Royal Medical Services (RMS) where the malarious patients were treated.

Results From the 142 participants, 52.1% used Mefloquine for prophylaxis in comparison with Doxycycline which was used by 29.6% of them, and the rest, 18.3%, used more than one prophylactic method. One case of malaria infection occurred during the study period and it was diagnosed as Severe Falciparum Malaria (SFM). The patient answered that he didn't use any prophylactic medication, Cost 1 and Cost 2 evaluated and found to be £10189.00 and £1220.00 respectively.

Conclusion The study showed much less cost when using these drugs for prophylaxis by 94% per capita comparing with the cost of treating one case of Severe Falciparum Malaria (SFM).

Key words Malaria, Imported, Prophylaxis, Antimalarials, Costs.

1.0 INTRODUCTION

Although malaria was eradicated in Jordan many years ago, it is currently being imported in Jordan by those Jordanians who have participated in UN medical missions within the Peace Keeping Forces (PKF) in different parts of the world, mainly in Africa, and Asia.

The problem of malaria is considered to be a major public health problem around the world. This serious disease continues to affect mostly poor nations. Being free from malaria is a fundamental right of humankind, but the disease still among the top ten killer diseases in the world [1]. The World Health Organization's Annual estimates vary between three hundred million to five hundred million cases of malaria and the numbers of deaths are estimated to be from 1.5 million to 2.7 million deaths worldwide. The vast majority of these cases occur in Sub-Saharan tropical countries, while outside Africa, 2/3 of the cases occur in just three countries which are India, Brazil, and Sri Lanka. However, malaria exists in about 100 countries [1] .

This serious disease becomes in sometimes fatal disease which is widespread in many tropical and Sub-Saharan tropical countries. It affects about 40% of the global population [2] , It is transmitted by being bitten by an infected mosquitoes that are carrying the malaria parasites in their saliva.

The continuous travel to regions where malaria is endemic there leads to an increase of imported cases, especially if prophylactic methods used are not strictly followed [3] .

1.1 Aim.

In this research, the study sample used members of the Jordanian Armed Forces (i) Who took antimalarial drugs as prophylaxis to protect them from being infected by malaria, and (ii) Other participants who did not used prophylactic medicines or the prophylactic regimen was not strictly followed and as a result became infected with malaria.

This research project aimed to evaluate the cost of using drugs to combat an established infection as compared with drugs used for prophylactic purposes.

1.2 Objectives

The overall aim of this project was to investigate the cost of prophylaxis of malaria in Royal Medical Services (RMS) staff of Jordanian Armed Forces (JAF) in Peace Keeping Forces (PKF) of the United Nations (UN) as compared with the treatment of the disease in those who did not take prophylaxis. This was achieved using the following objective:

(i) To estimate the cost of using anti-malarial drugs as treatment compared to them as prophylaxis.

That have been done by estimating, evaluating, and calculating the data collected from the sample study and the research done, and comparing the results obtained then we can find out and discuss

the cost of using antimalarial drugs as treatment compared to using them for prophylaxis.

2.0 Methods :

The participants of this study were 178 subjects (*n*=178) went to Liberia (West Africa) on early February 2012 and spent about six months in that area. The participants are working among the Jordanian (JORMED) Level III Hospital within the United Nations Mission in Liberia (UNMIL). An informed consent has been obtained from DRMS Ethics Committee. A soft copy of the questionnaire was sent to the pharmacist in the hospital who was responsible for enabling the participants to fill it. The soft copy was uploaded to PC in the pharmacy and every participant was able to fill it on that PC. 142 subjects filled in the questionnaire; a response rate was 79% (142/178). The antimalarial drugs prices used in this study was gathered from the records of Royal Medical Services' inventories and Tender Department, and the cost of treating a malaria patient was gathered from the records of financial offices in the hospitals of Royal Medical Services, the currency used in these prices and costs data were in Jordanian Dinars, and it was converted to Sterling pounds according to the official inter-bank exchange rate at that time which was JOD 1.12 to £1. The participants have to take prophylactic medicine, or they will be at risk of acquiring malaria, the prophylactic medicine that have been taken by the participants will cost RMS a particular cost (Cost 1), whereas those who acquired malaria will need treatment and hospitalization and will cost the RMS another different cost (Cost 2), the diagram of the study flow is shown in Figure 1 below.

Cost 1 was evaluated and calculated according to the equations shown in table 1 (part A) below and Cost 2 was evaluated and calculated also according to the equation shown in the same table (part B), Cost 1 and Cost 2 were evaluated, calculated, and compared, and then the conclusion was built up according to the results found out.

Table1: Equations used in the study to calculate costs

Cost 2 was estimated, evaluated, and measured according to some cost categories which are:

(1) Direct costs (**DC**): which include all costs of treatment malaria such as medicines, medical instruments, hospitalization, and costs of medical staff.

(2) Indirect costs (**IDC**): these are the expenses related to the whole subject of treating malaria like treatment time, waiting time, travel costs, costs of transferring patient to hospital.

(3) Intangible costs (**IGC**): these are immeasurable costs resulted from the loses occurred due to the impact of malaria disease upon the life of the patient and of society like loses resulted due to the absenteeism of the patient from the work field, the loses resulted when the patient become unable to perform his tasks in the life during the disease period.

All the above three categories of cost was either calculated from the data collected from the records of RMS hospitals' financial offices, or estimated and will be added to the final value of the Cost 2 in the study.

3.0 Statistical Analysis:

Analyses were performed using the Statistical Package SPSS 9.0, and Excel. Data were reported as mean and standard deviation. A probability value of <0.05 was considered statistically significant. All *P* values were 2-tailed.

4.0 RESULTS:

During the study, 142 participants of a total of 178 subjects (*n*=142) were responded to our requisition to fill in the questionnaire (Response rate 79%). 138 males (97.2%) and 4 females (2.8%) subjects, their age ranged from 18 to more than 46 years. 43.7% of the participants who filled in the questionnaire worked in the hospital field which is the largest percentage.

86 participants (52.1%) used Mefloquine tablets as a prophylactic method against malaria, and 56 (29.6%) participants used Doxycycline capsules, 18.3% of the participants used in addition to these antimalarial drugs a physical method against malaria like mosquito nets and Insect Repellents, 46.2% of them used Mefloquine and Insect repellent while 53.8% of them used Doxycycline in addition to Insect Repellent as shown in figure 2.

118 participants (83.1%) claimed that they have received medical information and a training for the use of antimalarial drugs as a method of prophylaxis against malaria from the medical professional team in the mission, while 24 (16.9%) of them claimed that they have not received such training. Those who have used Mefloquine as a prophylaxis 37% of them answered correctly about the time of starting taking the first dose and 97.7% of them answered also correctly about the time of stopping taking the medicine after they will be back home. Whereas regarding those who used Doxycycline as a prophylaxis medicine, 83.9% of them answered correctly about the time of starting taking the first dose, while just 14.3% of them answered correctly about the time of stopping taking the medicine after they will be back home.

From those 86 participants who have used Mefloquine as a prophylaxis method 16 (18.6%) participants experienced some kinds of Mefloquine side effects, these side effects are summarized and listed in table 4 below. While the numbers of participants who experienced these side effects are presented in figure 7, which shows that the most frequent side effect was strange sleep dreams (24.2%), followed by Hallucination and Tiredness which occurred in about (15.2%) of them, while Night disturbances, Muscle Aches, and Stomach pain occupied the third frequent side effects by about (9.1%). From those 56 participants who used Doxycycline as a prophylaxis method, 50 (89.3%) participants claimed that it was happened with them once or more that they forgot to take a dose of doxycycline capsule.

A List of Antimalarial drugs used in Jordan Royal Medical Services Hospitals and their prices were collected from the records of the Directorate of Royal medical services / Directorate of Pharmacy and Drugs – Medicines' Tenders Group. The prices were in Jordanian Dinars and they were converted to Sterling pounds according to the official inter-bank exchange rate at that time which was JOD 1.12 to £1 (Table 5).

Just one case of malaria was reported during the study period which occurred during the sixth month of the period, and the case suffered from respiratory distress, and severe anemia (Hb 4.3 gm/dl), in addition to other malaria symptoms. The patient answered that he didn't use any prophylactic medication, The case was diagnosed as severe falciparum malaria (SFM).

The quantities and prices of the Antimalarial drugs which have been used either for the prophylaxis against of malaria or for the treatment of the reported malaria case were filled in the (table 6) below, and the costs were calculated according to the equations which have been explained previously in table 1 in the section of study population and design.

The hospitalization costs in table 6 above included the Direct costs (**DC**) which are the costs of medicines used for the treatment of malaria plus the costs of hospital admission for 10 days and the costs of other medicine used for palliative care, the cost of medical instrument and disposable used and other expenses, these figures were supplied by the financial office in the JORMED Level III Hospital. The Indirect costs (**IDC**) included the travel costs needed for the evacuation of the patient to Jordan in case of non-responding to the treatment. The Intangible costs (**IGC**) resulted from the absenteeism of the patient from his work field for 20 days and being unable to perform his duty in the security field of the hospital and the effect of his absence on his colleagues who have to fill the position which has been left empty due to the patient absence.

Tables:

Table 1: Equations used in the study to calculate costs

Part A

No	Equation	No. of tablets used	Price JOD/tab	Total Cost (JOD)	Total Cost (£)
1	(# of participants used Mefloquine) X (# of weeks) = Result A (**RA**)	**RA**	Price collected from Data	**RA** X Price = Result B **(RB)**	**RB** X ER (Exchange rate)
2	(# of participants used Doxycycline) X (# of days) = Result C (**RC**)	**RC**	Price collected from Data	**RC** X Price = Result D **(RD)**	**RD** X ER (Exchange rate)
3	# of participants used Insect Repellant) X (# of months) = Result E (**RE**)	**RE**	Price collected from Data	**RE** X Price = Result F **(RF)**	**RF** X ER (Exchange rate)
				Part A Grand Total (£)	**Cost 1**

Part B

No		No. of tablets used	Price JOD/tab	Cost of Hospita-lization	Total Cost (JOD)	Total Cost (£)
1	(# of participants Acquired Malaria) X (# of tablets and ampules used) =Result G (**RG**)	**RG**	Price collected from Data	Cost collected from hospital Data (**RH**)	(**RG** X Price) + **RH** = Result J (**RJ**)	**RJ** X ER (Exchange rate)
					Part B Grand Total (£)	**Cost 2**

Table 2: Numbers of Participants (and percentages) participated in the study.

	Age Group				**Gender**	
	18-25	**26-35**	**36-45**	**46-above**	**Male**	**Female**
Number of Participants	50	51	29	12	138	4
Percentage	35.2%	35.9%	20.4%	8.5%	97.2%	2.8%

	Work			**Educational Degree**			
	Field	**Hospital**	**Administration**	**↓Tawjihi**	**Tawjihi**	**BSc**	**Higher Education**
Number of Participants	46	62	34	0	51	91	0
Percentage	32.4%	43.7%	23.9%	0.0%	35.9%	64.1%	0.0%

Table 3: Number of Participants who have received medical information and training about the using of Antimalarials.

Have you received any information about methods of prophylaxis and regimen of taking medicines from medical professional in your team?	**No. of Participants**	**Percentage**
Yes	118	83.1
No	24	16.9
Total	142	100.0

Table 4: List of Mefloquine Side effects experienced by some participants expressed in order of occurence.

No	Side Effect	%
1	Strange Sleep Dreams	24.2%
2	Hallucination	15.2%
3	Tiredness	
4	Night Disturbances	9.1%
5	Stomach Pain	
6	Muscle Aches	
7	Loss of Appetite	
8	Loss of Concentration	
9	Diarrhoea	
10	Nausea	

Table 5: List of Antimalarial drugs in JRMS and their prices.

No	**Drug**	**Price JOR / Unit dose**	**Price £ / Unit dose**
1.	Artemether – Lumefantrine 20mg/120mg tablets	1.051	0.94
2.	Primaquine tablets 15mg tablets	0.745	0.67
3.	Quinine 600mg/2ml ampules	8.493	7.58
4.	Doxycycline 100mg capsules	0.120	0.11
5.	Clindamycine 150mg capsules	0.174	0.16
6.	Mefloquine 250mg tablets	2.521	2.25
7.	Insect Repellent Roll Stick bottles	1.100	0.98

Table 6: calculations of costs.

Part A

No	Equation	No. of tablets used	Price JOD/tab	Total Cost (JOD)	Total Cost (£)
1	Mefloquine tablets: 86 X 31	2666 tab	2.521	6720.986	7528.00
2	Doxycycline capsules: 56 X 214	11984 cap	0.12	1438.100	1611.00
3	Insect Repellant bottles: 142 X 6	852 bottle	1.100	937.200	1050.00
			Part A Grand Total (£)		**Cost 1 = £10189.00**

Part B

No	Equation	No. of tablets used	Price JOD/tab	Cost of Hospita-lization	Total Cost (JOD)	Total Cost (£)
1	1 X (39 ampules Quinine + 12 tablets Artemether and Lumefantrine).	39 amp 12 tab	8.493 (amp) 1.051 (tab)	(343.839) + (745.000) **DC** (0.000) **IDC** (0.000) **IGC**	1088.839	**1220.00**
				Part B Grand Total (£)		**Cost 2 = £1220.00**

(**DC**: Direct Costs, **IDC**: Indirect Costs, **IGC**: Intangible Costs).

Table 7: Summary of the Malaria Treatment Policy in Jordan 2011 [4]

No	Type and Species of Malaria	First line Treatment	Second line Treatment
1	Uncomplicated P. falciparum malaria (UCFM)	**Art-Lum** (3 days) followed by **PQ** (one single dose)	**QN** plus **Dox** (7 days)
2	Severe P. falciparum malaria (SFM)	**QN** Intravenous Infusion followed by **Art-Lum** (3 days)	
3	P. vivax and P Ovale malaria	**CQ** (3 days) followed by **PQ** (14 days)	**Art-Lum** (3 days) followed by **PQ** (one single dose)
4	P. malariae malaria	**CQ** (3 days) followed by **PQ** (one single dose)	
5	Mixed infection of P. falciparum with P. vivax or P. ovale	**Art-Lum** (3 days) followed by **PQ** (14 days)	
6	Mixed infection of P. falciparum with P. malariae	**Art-Lum** (3 days) followed by **PQ** (one single dose)	

(**Art-Lum**: Artemether-Lumefantrine, **PQ**: Primaquine, **QN**: Quinine, **Dox**: Doxycycline, **CQ**: Chloroquine).

Table 8: comparison of Cost 1 and Cost 2 (per capita).

	Cost 1	Cost 2
Total Amount £	10189.00	1220.00
Amount £ per capita	71.75	1220.00
% saved by Prophylaxis	94%	
	The cost of treating one malaria case is 17 times more expensive	

Figures:

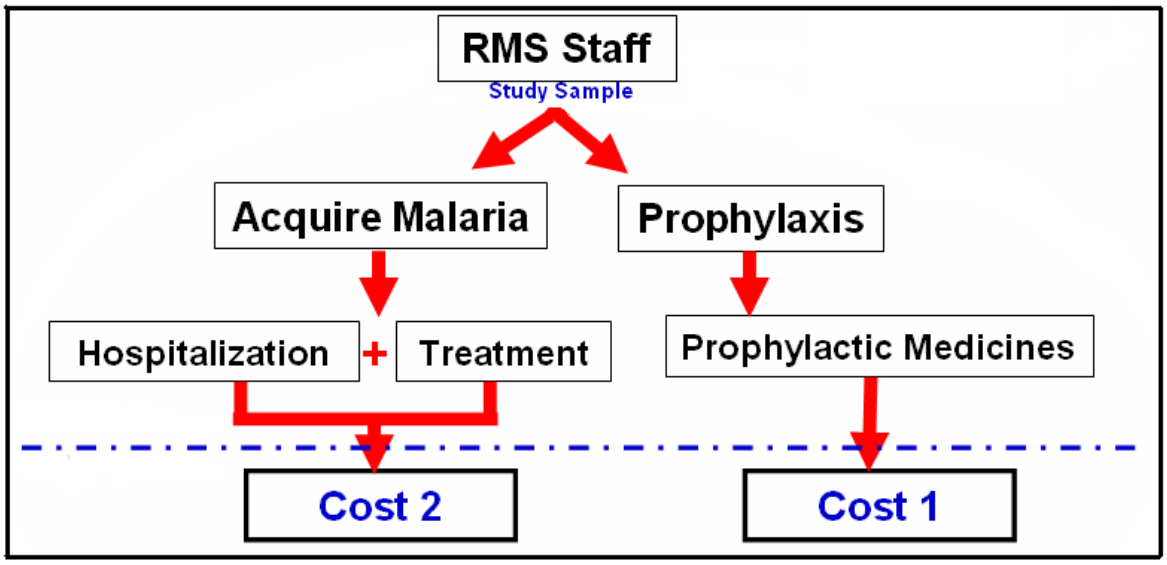

Figure1: study design flow diagram. RMS : Royal Medical Services

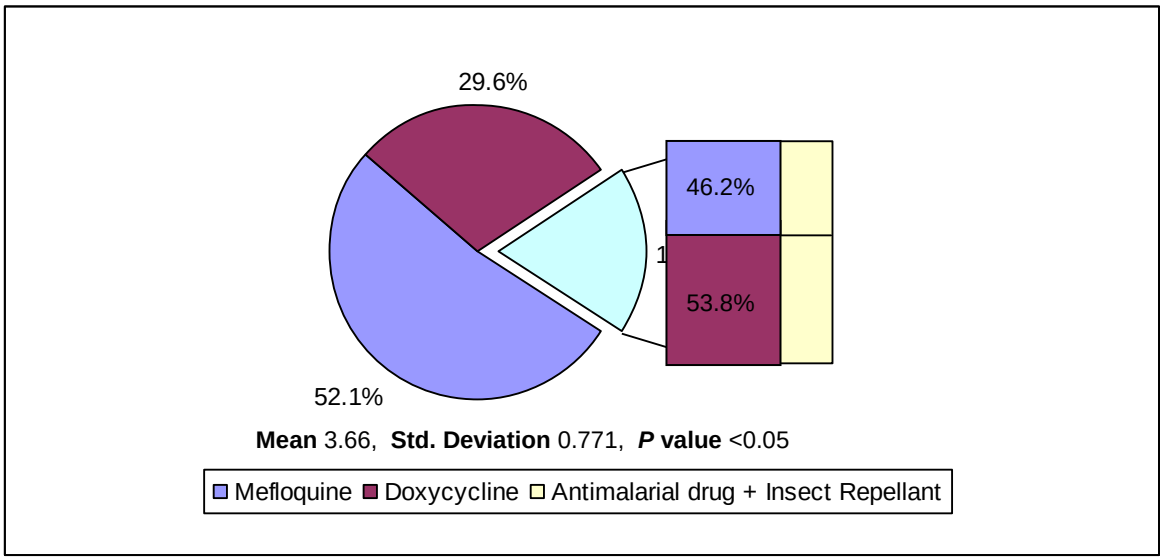

Figure 2: Prophylactic methods against malaria used in the study.

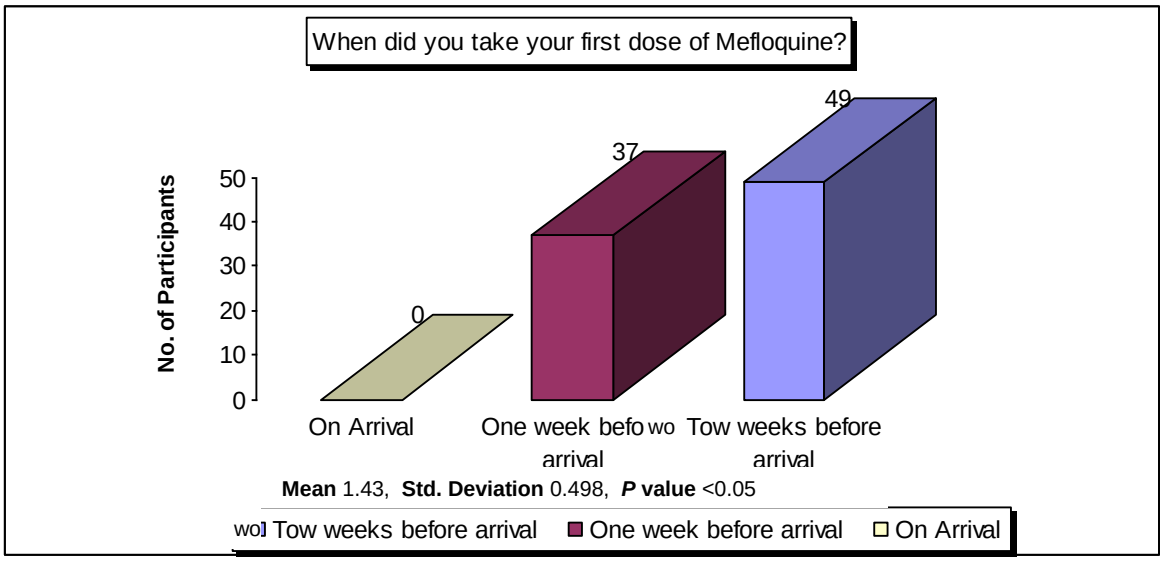

Figure 3: The time of taking first dose of Mefloquine when using it for prophylaxis against malaria (the correct answer is One week before arrival).

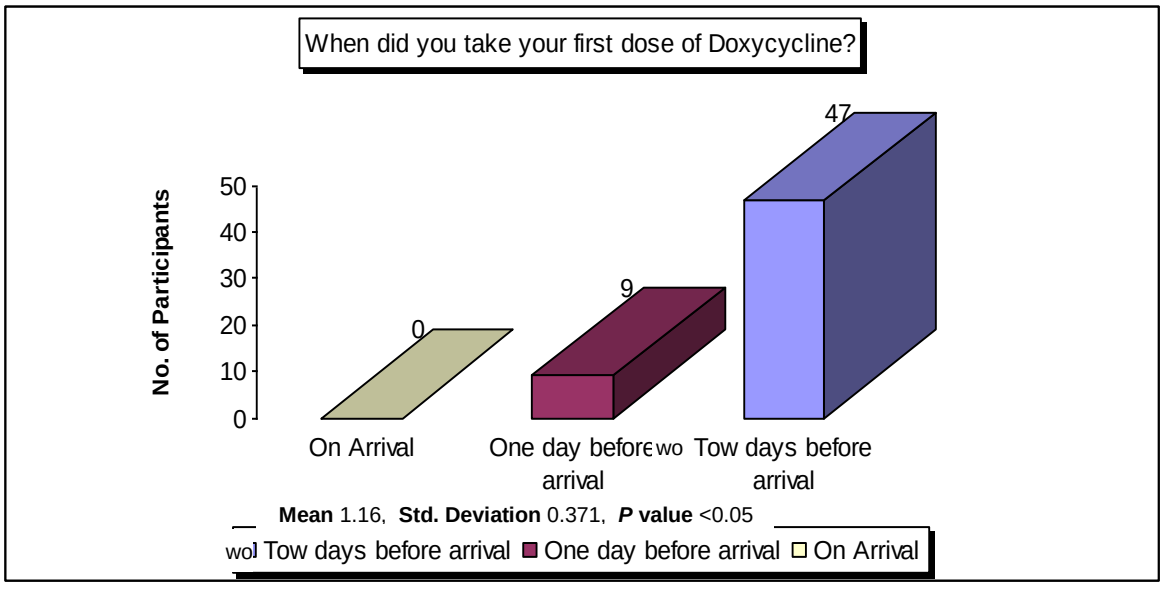

Figure 4: The time of taking first dose of Doxycycline when using it for prophylaxis against malaria (the correct answer is two days before arrival).

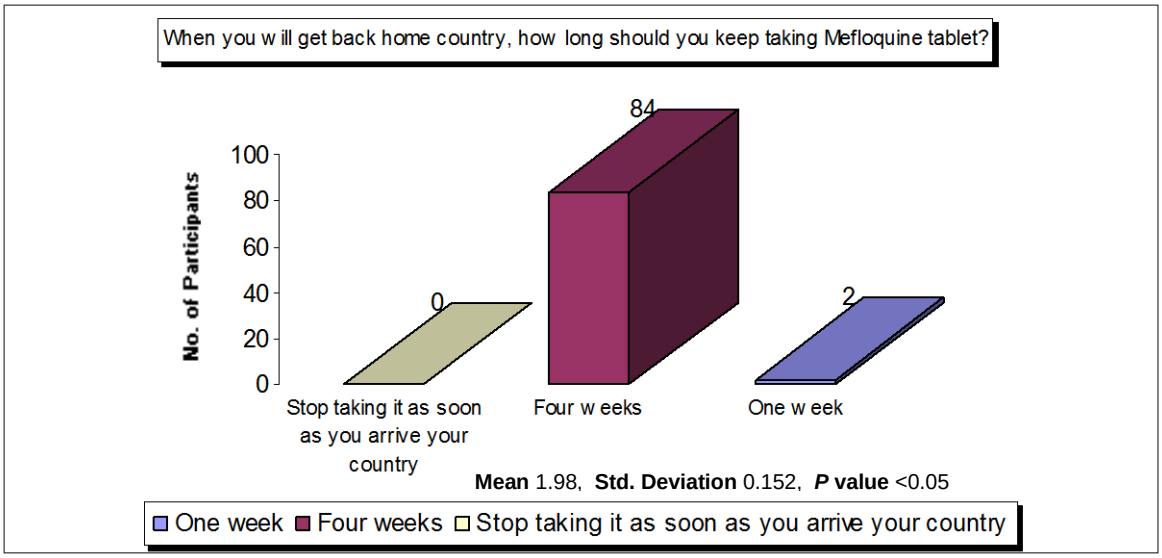

Figure 5: the time of stopping taking Mefloquine when using it for prophylaxis against malaria (the correct answer four weeks after arrival).

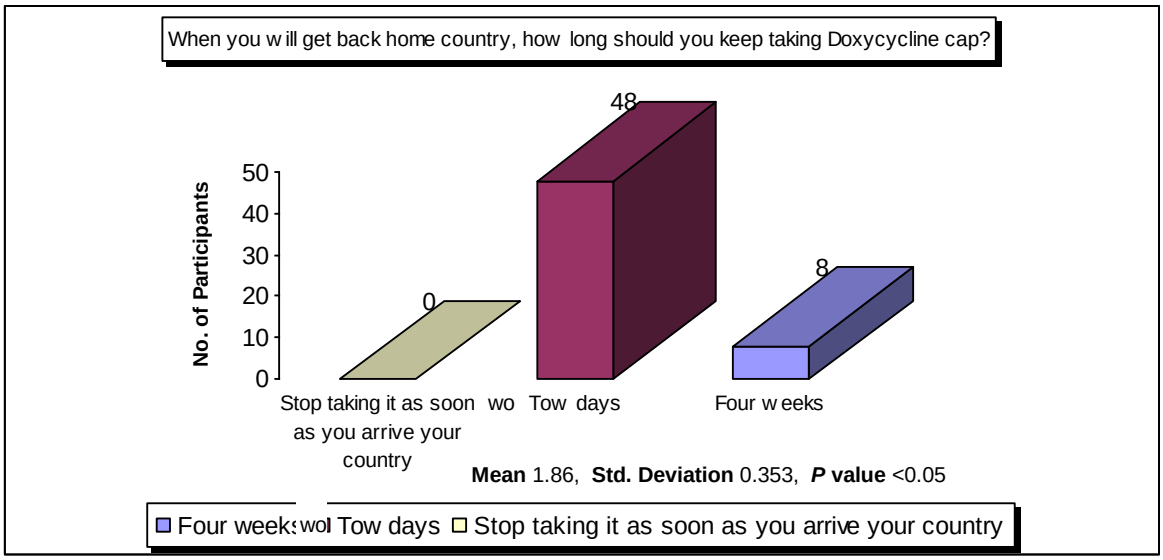

Figure 6: the time of stopping taking Doxycycline when using it for prophylaxis against malaria (the correct answer four weeks after arrival).

5.0 DISCUSSION:

The vast majority of the participants (52.1%) used Mefloquine for prophylaxis in comparison with Doxycycline which has been used by (29.6%) of the participants and the rest (18.3%) used more than one prophylactic method. Using Mefloquine is much easier than Doxycycline because it is easier to take one tablet weekly than taking it daily. This was appeared obviously in those who used doxycycline when (89.3%) of them forgot to take one dose or more in several times.

The problem with using Mefloquine is its side effects which appeared in (18.6%) of participants who were using it. Even though these side effects ranged from mild stomach upset or muscle pain to strange sleep dreams and hallucination in some cases, all of them disappeared immediately when the participants stopped taking Mefloquine and changed to Doxycycline.

Many participants 83.1% confirmed that they have received a medical information and a training for the use of antimalarial drugs for prophylaxis against malaria, but the outcome of the training showed relatively low percentages of correct information when they answer about the use of these drugs, such as 37% of them answered correctly about the time of starting taking the first dose of Mefloquine, and just 14.3% of them

answered correctly about the time of stopping taking Doxycycline after they will be back home.

During the study period, fortunately, only one person from the 142 participants acquired malaria, which occurred during the sixth month of the period. The individual suffered from Respiratory distress, and severe anemia (Hb 4.3 gm/dl) <5 gm/dl, in addition to other malaria symptoms such as fever and malaise. The case was diagnosed as severe falciparum malaria (SFM). The malaria case was treated according to Malaria Treatment Policy used in Jordan (Table 7) which is also compatible with the regimen of treatment of malaria explained in British National Formulary. The patient was given Quinine IV (20mg/kg Loading Dose over 4 hrs) then (10mg/kg q8hrs) for 6 days (5-7 days), then it followed by Artemether – Lumefantrine 20mg/120mg tablets (4 tablets once a day) for 3 days.

Table 7: Summary of the Malaria Treatment Policy in Jordan 2011 [4] .

The cost of prophylaxis used by the participants of this study (**Cost 1**) is measured by calculating the prices of used Mefloquine tablets and Doxycycline capsules and insect repellant bottles during the study period which calculated as 31 weeks for Mefloquine users (26 weeks + 1 weak pre-period + 4 weeks post-period). The study period for Doxycycline users has been calculated as 214 days (184 days + 2 days pre-period + 28 days post-period). While for the Insect repellant, each participant received one bottle of insect repellant every month, so the study period was considered 6 months for all participants despite the fact that some of them have not used any. All prices used are the prices of the medicines purchased through the Tenders of Royal Medical Services (Table 5), so they are tender prices not market prices and this is the reason why they are cheaper than the prices of the private markets. All the above calculations are shown in Table 6.

The cost of treating the malaria case (**Cost 2**) in Table 6 is calculated by measuring the three categories of cost, the Direct costs (DC), Indirect costs (IDC), and the Intangible costs (IGC). The DC calculated by measuring the cost of the treatment which he has received in the hospital according to the same medicines prices listed in Table 5 (343.839 JOD), in addition to the costs of hospital admission for 10 days (745.000 JOD) which is supplied by the Financial office in the JORMED level III hospital.

The IDC in this study could be the travel costs if the patient did not responded to the available treatment and have to be evacuated to Jordan by the UN flights which would be on the expense of the RMS. The IGC could be the costs resulted from the losses happened by the patient's absence from his duty field in hospital security. IDC and IGC considered (0.000 JOR) because it was difficult to be measured or estimated according to the little information available.

In comparing (Cost 1) and (Cost 2), which is the target of my study, as shown in Table 8 we can find that the cost needed to achieve prophylaxis against malaria for 142 participants was **£10189.00** which is about **£71.75 per capita,** while it was **£1220.00** for the treatment of one case of SFM.

$$\% \text{ saved by prophylaxis} = \left[1 - \frac{\text{Cost of Prophylaxis per capita}}{\text{Cost of Treatment per capita}} \right] \times 100\ \%$$

$$\% \text{ saved by prophylaxis} = \left[1 - \frac{71.75}{1220.00} \right] \times 100\ \%$$

$$\% \text{ saved by prophylaxis} = 94\%$$

$$\text{Times saved by prophylaxis Vs. treatment} = \frac{\text{Cost of Treatment per capita}}{\text{Cost of Prophylaxis per capita}}$$

$$\text{Times saved by prophylaxis Vs. treatment} = \frac{1220.0}{71.75}$$

Times saved by prophylaxis Vs. treatment = 17 Times

Table 8: comparison of Cost 1 and Cost 2 (per capita).

6.0 Weakness of the study and problems faced.

6.1 The case of malaria investigated in this study was a SFM which needed hospital admission for treatment, but this is not always the case, some uncomplicated malaria cases do not need admission for treatment, they just need taking antimalarial drugs at home, and the treatment of these cases costs much less than what the treatment of this case did.

6.2 In the calculations done for the cost in prophylaxis we have not mentioned the calculation of costs of side effects such as (the absence from work, another drugs used for decreasing symptoms of side effects… etc.) also the indirect and intangible costs as done in treatment group.

7.0 CONCLUSION

Although malaria was eradicated in Jordan many years ago, it is still being imported to Jordan by those Jordanians which are participated in UN medical mission within the Peace Keeping Forces in different parts of the world, mainly Africa, and Asia.

In this study, the investigation included a study sample of RMS staff participated in the UN mission in one of the high malaria endemic area in which the participants used Antimalarial drugs for the prophylaxis against malaria, and the study showed much less cost when using these drugs for prophylaxis by 94% per capita comparing with the cost of treating one case of Severe Falciparum Malaria (SFM).

This reduction of this cost may reduce the overall costs and loss of money in the general budget of the RMS paid for health services, the same idea could be implemented on the health system in Jordan as this will lead to increase the amount of money available for the health system in the country to improve other services and to implement health projects that produce good base of health in the country.

The effect of malaria on the health system in Jordan appeared clearly since a long time, and it affected negatively the health system in Jordan in past and that is what lead Jordanian Ministry of Health to start eradicating it and taking action against it since the mid of last century.

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