Ministry of National Health Services,
Regulation and Coordination,
Government of Pakistan

DMC

G6PD SCREENING

PILOT ACTIVITY REPORT

Prepared by

Dr. Mariam Ashraf

Dr. Inam Kakar

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ACRONYMS AND ABBREVIATIONS

CO-PR	Co-Principal Recipient
CQ	Chloroquin
DMC	Directorate of Malaria Control
DHQH	District Headquarter Hospital
DHIS	District Health Information System
FATA	Federally Administered Tribal Areas
G6PD	Glucose 6 Phosphate Dehydrogenase
GSH	Glutathione Stimulating Hormone
KP	Khyber Pakhtunkhwa
NADP	Nicotinamide Adenine Dinucleotide Phosphate
P. FALCIPARUM	Plasmodium Falciparum
P.VIVAX	Plasmodium Vivax
PQ	Primaquin
RDT	Rapid Diagnostic Tests
SRS	Sub- Recipient
TGF	The Global Fund
TIH	The Indus Hospital
WHO	World Health Organization

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1 INTRODUCTION AND BACKGROUND

1.1 GLUCOSE 6 PHOSPHATE DEHYDROGENASE (G6PD)

G6PD is a cytoplasmic enzyme involved in prevention of cellular oxidative damage by stimulation of detoxification of free radicals. It catalyzes the production of Nicotinamide Adenine Dinucleotide Phosphate (NADP), which is necessary for maintenance of reduced levels of Glutathione Stimulating Hormone (GSH) important to protect erythrocytes from oxidative damage and to reduce susceptibility to hemolysis[1].

1.2 G6PD DEFICIENCY

G6PD deficiency is a genetic disorder that occurs most often in males. This condition mainly affects red blood cells, which carry oxygen from the lungs to tissues throughout the body. In affected individuals, a defect in the enzyme G6PD causes red blood cells to break down prematurely. This destruction of red blood cells is called hemolysis. The most common medical problem associated with G6PD deficiency is hemolytic anemia, which occurs when red blood cells are destroyed faster than the body can replace them[2].

1.2.1 Prevalence of G6PD deficiency

It is prevalent throughout Africa, Asia, Southeast Asia and parts of South America, where malaria is endemic. The estimated proportion of individuals carrying a G6PD deficiency gene varies from 5% to as much as 33% in different parts of sub-Saharan Africa and Asia[3]. It has hugely diverse mutant phenotype and genotype and affects 400 million people worldwide. The recent WHO G6PD deficiency prevalence map (refer to figure 1) has categorized Pakistan in regions with low G6PD activity.

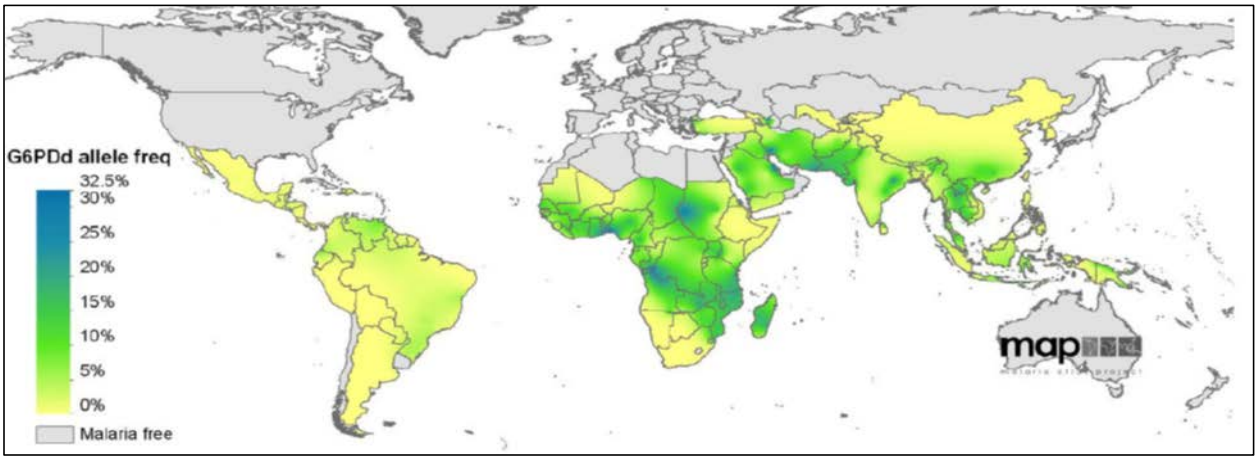

Figure 1: G6PD prevalent populations[4]

1.3 PRIMAQUINE AND G6PD DEFICIENCY

Malaria eradication is only possible with serious attempts to address asymptomatic infection and chronic infection by both Plasmodium Falciparum (P.falciparum) and P.vivax). Currently available drugs that can completely clear a human of P.vivax (known as "radical cure"), and that can reduce transmission of malaria parasites, are those in the 8-aminoquinoline drug family, such as Primaquine (PQ) which is potentially useful for malaria control and elimination. Unfortunately, people with glucose-6-phosphate dehydrogenase (G6PD) deficiency risk having severe adverse reactions if exposed to these drugs at certain doses.

G6PD deficiency is the most common human enzyme defect, affecting approximately 400 million people worldwide. Scaling up radical cure regimens will require testing for G6PD deficiency, at two levels: 1) the individual level to ensure safe case management, and 2) the population level to understand the risk in the local population to guide P.vivax treatment policy. Several technical and operational knowledge gaps must be addressed to expand access to G6PD deficiency testing and to ensure that a patient's G6PD status is known before deciding to administer an 8-aminoquinoline-based drug[5].

Primaquine is currently the only medication used for radical cure of P.vivax infection. Unfortunately, its use is not without risk. Patients with G6PD deficiency have an increased susceptibility to hemolysis when given PQ. This potentially fatal clinical syndrome can be avoided if patients are tested for G6PD deficiency and adequately informed before being treated[6].

According to the national malaria treatment guidelines for P.vivax malaria treatment, PQ must be administered for 14 days at a daily dose of 15 mg/day in combination with Chloroquine (CQ) at a total dose of 25 mg/kg ,where not contraindicated.

2 RATIONALE, AIM AND OBJECTIVES

2.1 RATIONALE

Use of Primaquine is the mainstay for radical treatment of P.vivax malaria cases in Pakistan. In Pakistan, previous studies have point out a variable 5-7% G6PD deficient activity in Pashtun ethnic groups near Afghanistan border[7]. However, there is a lack of evidence on haemolysis associated with PQ treatment in Pakistan, even though more than 72% of the malaria cases are caused by P.vivax and are being treated with PQ for the last 25 years.

Based on the importance to have some evidence about G6PD deficiency presence in Pakistan, Directorate of Malaria Control (DMC), planned a small scale pilot activity for screening the patients visiting public sector health facilities for G6PD deficiency. This study was carried out to identify the frequency of G6PD deficiency and operational barriers in introducing G6PD screening at a larger scale for better case management of the *P. Vivax* malaria cases.

2.2 AIM

Ensuring testing for G6PD deficiency for safe use of Primaquine in radical cure of P.vivax malaria in Pakistan.

2.3 OBJECTIVES

The objectives of the pilot were to;

1. Assess the operational modalities for rolling out Point of Care Rapid Diagnostic Tests (RDTs) to measure G6PD deficiency in confirmed P.vivax cases.
2. Identify methodological priorities to support development of appropriate G6PD testing strategies in support of P.vivax radical cure.

3 METHODOLOGICAL STRATEGY

3.1 STUDY AREA AND SAMPLE SIZE

The pilot was carried out in the District Headquarters (DHQ) hospitals sentinel sites of the 16 interventions districts and agencies of TGF grant from Balochistan, Sindh, KP and FATA from 1st October to 31st December 2016.

A total of 4000 RDT kits for G6PD screening were utilized for conducting the pilot. WHO had provided these kits for the pilot study. 250 RDTs were used at each sentinel site in different provinces/regions initially and then were distributes according to high burden districts. DHQs were selected because of high case load as greater population seek services from the health facility and better diagnostic facility (Microscopy) availability.

The names of the districts/agencies selected from each province/region are shared in table1

Table 1: Districts selected for the Pilot

S#	BALOCHISTAN	S#	SINDH	S#	KP	S#	FATA
1.	Zhob	2.	Mir Pur Khas	3.	D. I. Khan	4.	Kurram A
5.	Noshki	6.	Khairpur	7.	Lakki Marwat	8.	Khyber A
9.	Pishin	10.	Thatta	11.	Mardan	12.	South Waziristan
13.	Sibbi					14.	Bajuar Agency
15.	Kech						
16.	Jaffar Abad						

3.2 STUDY POPULATION

Those patients presenting at the public facilities / DHQ hospitals with fever and diagnosed / confirmed as malaria cases were selected for the study in the 16 targeted districts.

3.3 STUDY PHASES

The study was carried out in the following phases:

a) Training of the focal persons
b) Site preparation and provision of the G6PD kits
c) Screening of patients for and recording results
d) Monitoring and supervision
e) Data entry and cleaning
f) Data analysis
g) Report writing

3.4 SCREENING TEST

G6PD detecting RDTs have been developed more recently. RDTs are lateral flow chromatographic tests that offer rapid qualitative detection using cheap, simple methodology that can be successfully followed after training. RDTs can be tested from a finger prick sample, do not require specific equipment and can be performed at point of care to allow prompt determination of G6PD deficiency status prior to safe administration of treatment. The RDT is comprised of a nitrocellulose strip housed inside a plastic cassette. Blood, followed by buffer are added to the RDT, and then a 10 minute incubation step is observed to allow the sample to wick the length of the nitrocellulose strip. Normal G6PD activity is indicated when nitro blue tetrazolium (impregnated on the nitrocellulose strip) is reduced to formazan which is purple. G6PD deficiency is identified through lack of a color change, the strip remains white[8]. These RDTs have been used for screening G6PD deficiency among the given population.

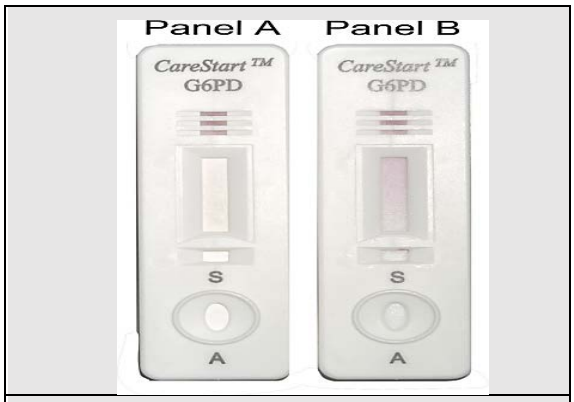

Figure 2: RDT used for screening in the pilot

Table 2: Interpretation of G6PD results
How to read the results?
Positive: G6PD Deficient: No color change or very faint purple color **Normal:** A distinct purple color **Invalid:** Test results are invalid either there is no blood flow or incomplete blood flow at the time of reading

3.5 DATA COLLECTION

Blood samples were taken from all the confirmed malaria cases coming to the OPDs of the targeted public health facilities and RDT screening for G6PD was carried out. Data was recorded of all positive malaria cases regardless of their species. This helped in estimating G6PD deficiency amongst *P.* vivax patients. Data was recorded for both groups deficient and not deficient in the data recording tool. The information of the malaria cases was recorded in the FM-1 registers as per routine practice for all the screened patients. Each screened patient was given a result card containing information regarding his G6PD deficiency status. Data was shared by sentinel site focal person with DOMC technical team on monthly basis.

Following standard procedures were followed

- Patients confirmed as malaria vivax cases whose G6PD status was yet not known were identified for G6PD deficiency
- Based on G6PD deficiency test, the dosage of PQ was determined and prescribed; and
- Treatment adherence and monitoring of adverse effects at the facility were followed (dependent on the follow up of the patients)

3.5.1 Data Recording Form

Information was collected and recorded on a structured data recording form (Annexure 1). The data recording form was developed in consultation with focal person of World Health Organization (WHO) Pakistan, and technical experts from the Directorate of Malaria Control (DOMC), Islamabad and The Indus Hospital (TIH).

4 TRAINING AND DATA COLLECTION

4.1 TRAINING ON G6PD SCREENING

One day training was carried out on 17th August 2016 in NACP Hall, NIH Islamabad. One focal person from each sentinel site (total of 16 participants) were trained. The training was conducted by WHO focal person Dr. Qutbuddin Kakar (National Professional Officer). It mainly focused on ***Protocols for screening of G6PD deficiency Using RDT Kits.***

Figure 3: Training for G6PD screening at DOMC

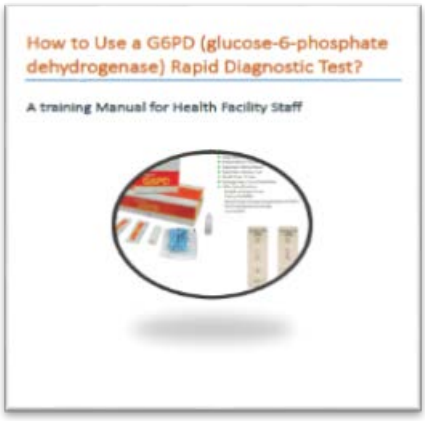

Figure 4: Training Manual for G6PD screening

A training manual was also developed by the WHO focal person. The purpose of this manual (refer to figure 4) was to train health workers to use G6PD Rapid Diagnostic Tests (RDTs) safely and effectively, during the management and treatment of P.vivax infection. Soft copies of all handouts and other related training support was also provided to the participants.

4.2 DATA COLLECTION AND ANALYSIS

Data was collected on prescribed forms simultaneously from the 16 sentinel sites in the four provinces/regions by the trained focal persons over a period of 4 months (Sep-Dec 2016). The focal persons shared the data with DMC regularly on monthly basis for the study duration. The focal persons faced some issues and challenges in the screening of malaria patients for G6PD deficiency which were catered during the study implementation. These issues and challenges during data collection have been discussed later in this report.

4.3 DATA ENTRY, CLEANING AND ANALYSIS

Data was entered and analyzed using SPSS. Descriptive analysis was done. Frequency and percentages of different variables were calculated and presented in form of tables and graphs.

5 ETHICAL CONSIDERATIONS

Verbal consent was taken from the participants who agreed to take part in the pilot. An explanation regarding G6PD testing was provided. The anonymity and confidentiality of the study participants were maintained throughout the study. The patients found with the G6PD deficiency in *P. Vivax* positive cases were given Primaquine as per the WHO guidelines with strict vigilance to jaundice.

6 LIMITATIONS OF THE STUDY

1. It should be flagged that this pilot is not the basis to assess the prevalence of G6PD deficiency in the selected sites as it was carried out in limited districts and within a limited time frame.

2. Fluorescence spot test (FST) is the most sensitive test for diagnosing G6PD deficiency especially in Asia[9, 10]; however it was not used due to the non-availability of FST in Pakistan.

3. The Care Start G6PD deficiency RDT kit produces a purple color to differentiate between normal and deficient subjects. Borderline results also produce a pale purple color. This can result in misinterpretation of RDT results by the screening person.

4. Based on the operational issues and challenges faced by the implementation team one day training was not enough as lots of issues were faced by the field teams and it was realized that at least three day training along with field testing should be carried out for planning such researches/testing.

7 FINDINGS

The pilot was mainly run to identify and understand the operational challenges which could be faced in introducing G6PD screening in the health facilities. A number of operational issues have been identified which are discussed later in this report. The key findings regarding G6PD deficiency in 16 sentinel sites (DHQH) of the selected districts by DOMC are shared below.

7.1 G6PD FINDINGS

Out of a total of 4000 kits which were provided for the pilot, 3805 (95%) kits were utilized for screening the patients. Overall 42 were found to be G6PD deficient, 3671 were normal and 92 results were found to be invalid. The deficient cases makes up around 1% of the overall findings (Figure 5).

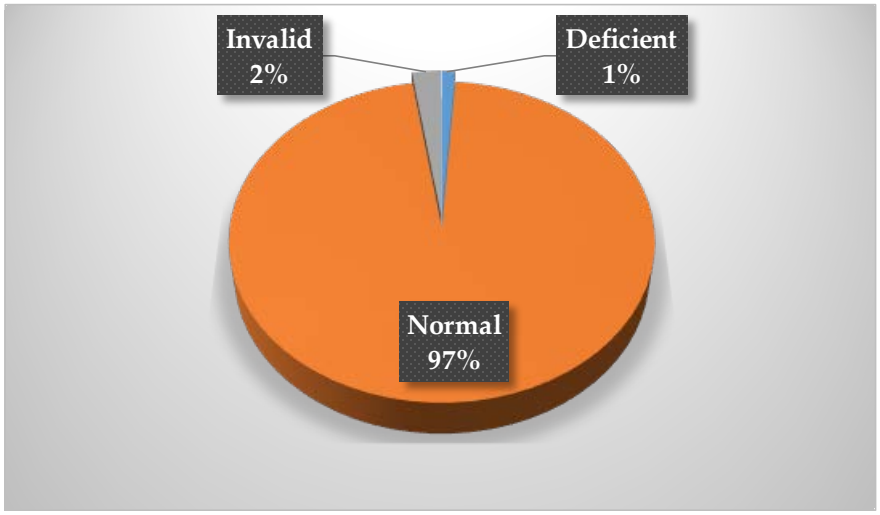

Figure 5: G6PD results

From the total deficient cases 24 (57%) were males and 18 (43%) were females. The average age of the screened patients was reported to be 25 years.

7.2 PROVINCIAL FINDINGS

Provincial breakdown indicates that highest number of cases were screened from Balochistan 1397 (37%), followed by FATA 916 (24%), Sindh 746 (20%) and KPK 746 (20%). Out of the 42 persons who were found to be G6PD deficient, 23 were reported from Balochistan, 14 from KP and 5 from FATA. None of the patients were found G6PD deficient in Sindh (Table 3).

Table 3: Provincial breakdown of G6PD pilot findings

	Screened		Deficient		Normal		Invalid	
Provinces	**F**	**%**	**F**	**%**	**F**	**%**	**F**	**%**
Balochistan	1397	37	23	55	1353	37	21	23
FATA	916	24	5	12	879	24	32	35
KP	746	20	14	33	713	19	19	21
Sindh	746	20	0	0	726	20	20	22
Total	**3805**	**100**	**42**	**100**	**3671**	**100**	**92**	**100**

7.3 DISTRICT FINDINGS

7.3.1 Findings from Balochistan

A total of 6 districts were selected form Balochistan. The kits were provided at DHQ as well as THQ hospitals. The rate of utilization of the kits was 93%. Highest number of G6PD deficient cases were reported form Zhob district (14) followed by Sibbi (9). From the rest of the district, none of the patients were reported to G6PD deficient. Results of 21 patients were reported to be invalid (Table 4).

Table 4: Findings from Balochistan

S. No	**Balochistan**	**Total no. of kits**	**Screened** *Frequency*	**Deficient** *Frequency*	**Normal** *Frequency*	**Invalid** *Frequency*
1.	Jaffarabad	250	216	0	211	5
2.	Zhob	250	249	14	235	0
3.	Pishin	250	220	0	220	0
4.	Noshki	250	214	0	214	0
5.	Sibbi	250	249	9	229	11
6.	Kech	250	249	0	244	5
	Total	**1500**	**1397**	**23**	**1353**	**21**

7.3.2 Findings from Khyber Pakhtunkhwa

In KP, the rate of utilization of kits was 99%. Three districts were selected from KP and from all the district G6PD deficient cases were reported. Highest cases were reported form Lakki Marwat (11). Two cases were reported from Dera Ismail Khan (D.I.Khan) and 1 from Mardan district (Table 5).

Table 5: Findings from Khyber Pakhtunkhwa

S. No	KP	Total no. of kits	Screened *Frequency*	Deficient *Frequency*	Normal *Frequency*	Invalid *Frequency*
1.	DI Khan	250	234	2	232	0
2.	Lakki Marwat	250	243	11	213	19
3.	Mardan	250	269	1	268	0
	Total	**750**	**746**	**14**	**713**	**19**

7.3.3 Findings from FATA

From FATA, 4 agencies were selected for the pilot. The rate of utilization of kits was 92% which is low as compared to other provinces. G6PD deficient cases were reported from only Bajaur agency (5). All other patients visiting the facilities were reported to have normal activity. Results of 32 patients were reported invalid (Table 6).

Table 6: Findings from FATA

S. No	FATA	Total no. of kits	Screened *Frequency*	Deficient *Frequency*	Normal *Frequency*	Invalid *Frequency*
1.	Kurram A	250	273	0	250	23
2.	Khyber A	250	239	0	239	0
3.	South.W	250	207	0	198	9
4.	Bajaur	250	197	5	192	0
	Total	**1000**	**916**	**5**	**879**	**32**

7.3.4 Findings from Sindh

In Sindh, 99% of the kits were utilized. Three high burden districts for P.vivax were selected, however, none of the districts reported any G6PD deficient case. Results of 20 patients were found to be invalid (Table 7).

Table 7: Findings from Sindh

S. No	Sindh	Total no. of kits	Screened *Frequency*	Deficient *Frequency*	Normal *Frequency*	Invalid *Frequency*
1.	Khair Pur	250	248	0	236	12
2.	Thatta	250	248	0	248	0
3.	Mir Pur Khas	250	250	0	242	8
	Total	**750**	**746**	**0**	**726**	**20**

7.4 ETHNIC DISTRIBUTION

Highest number of G6PD deficient cases were reported from Pashtuns (37) followed by Balochs (5). (Refer to table 8)

Table 8: Ethnic distribution of G6PD deficiency (n=3728)

S. No	Ethnic Group	Deficient *Frequency*	Normal *Frequency*	Invalid *Frequency*	Total *Frequency*
1.	Pashtoon	37	2069	55	**2161**
2.	Baloch	5	713	19	**737**
3.	Punjabi	0	2	0	**2**
4.	Sindhi	0	753	15	**768**
5.	Other	0	59	1	**60**

7.5 SIGNS AND SYMPTOMS OF THE PATIENTS PRESENTING IN THE FACILITY

Fever was the most common symptom which was reported by all the patients (100%). Other associated symptoms included nausea, vomiting, headache and general body weakness.

8 OPERATIONAL ISSUES AND CHALLENGES FACED DURING THE PILOT ACTIVITY

The operational issues identified during the activity right from beginning are discussed as follows

8.1 NEAR TO EXPIRY RDT KITS

During the implementation of the activities, questions were also raised about the quality of the kits. One main reason was the expiry dates of the kits which were within three month period time i.e. December 2016 and these were to be utilized as early as possible to prevent from expiry. Secondly,

8.2 INAPPROPRIATE SELECTION OF FEW SENTINEL SITES

Initially equal distribution of the G6PD kits was done. Initially, in some areas where P.vivax burden was low, rate of utilization of RDTs was reported to be very low. As a result new sites were selected and the RDTs were made available to those areas where P.vivax case load was high. This was done during the implementation of the activities. As a result delay in the pilot activity in some of the districts was noted as new sentinel sites were selected they were made functional and more staff was trained. Transferring of the kits from one province to another also added to the delay in activities.

8.3 GAPS IN TRAININGS, SELECTION AND CAPACITY OF THE STAFF TRAINED

It was identified that irrelevant persons were nominated for training who did not had adequate experience and skills to perform the test. Furthermore the quality of and duration of the training was also found to be inadequate as there were persons who were trained but were not able to perform the test properly. After selection of the new sites, new staff was trained by already trained staff and yet the quality of the step down training was not up to the standard as well. As a result the capacity of the personnel who were performing the test was not up to the standard.

8.4 DATA RECORDING AND REPORTING

The data recording forms were not filled properly by the focal persons and most of the information was found to be missing that hindered proper analysis. For instance microscopic results, treatment provided, follow up were not duly filled in. A lot of data was found missing.

8.5 WRONG READING OF THE G6PD DEFICIENT KITS

G6PD deficient kits of the sentinel sites when examined by the Principal Investigator and experts of DOMC and WHO, it was found that most of test results were invalid and not showing accurate results. However these were reported as G6PD deficient by field teams. This indicates the poor capacity of the teams who were trained to carry out the pilot.

8.6 LACK OF FOCUS ON PROPER MONITORING FOR QUALITY ASSURANCE

There were approved monitoring and supervisory visits planned to the pilot districts and agencies where the relevant officers could not conduct the desired number of monitoring visits. As a result the data received had a lot of issues.

8.7 DELAY IN SUPPLY OF RDT KITS

The activity was planned to commence simultaneously in each district and agency. It was reported that in some districts the activity started very late due to delay in the supply of RDT kits by the relevant SRs. In addition, due to selection of new sites the additional training and logistics added to the overall delay of the pilot activity.

Furthermore, for cross checking purpose, the kits with positive G6PD results were being transferred to DMC. Those with normal results were not transferred initially causing delays in the cross checking of the results for quality assurance.

9 DISCUSSION

Various studies highlight the importance of early diagnosis of Glucose-6-phosphate dehydrogenase deficiency as various research indicates that proper screening could avert the potentially harmful effect of the deficiency encountered during patient management with Primaquine. The danger of treating patients with drugs that are contraindicated for individuals with this deficiency could range from mild to severe hemolysis[11].

The results indicates that of the total sample selected only 1% of the sampled population was found to be G6PD deficient. The prevalence of G6PD deficiencies, which ranges from < 0.1% to > 15%, can significantly influence the population normal value[12]. Robust G6PD reference normal values for a given population can only be obtained using large sample numbers. When smaller sample numbers are used, the prevalence of severely deficient individuals may skew the population normal value. In practice, there is wide variability in how G6PD tests are evaluated[13].

Most of the cases were reported from Balochistan and among Pashtuns ethnic group. A previous study carried out has also identified majority of cases of phenotypic G6PD deficiency in Pashtun refugees in Pakistan originating from Afghanistan[14].

The key areas which need to be strengthened for future activities includes adequate training, nomination of trainers and trainee based on certain criteria. Proportionate sampling mainly involving high burden districts in which burden of P.vivax is high followed by adequate logistic and supervisory support. Monitoring and on field support also play an important role in adequate testing.

The studies indicate that ability to test for G6PD deficiency is also critical to current efforts for eradication of malaria. This holds true for Pakistan as well where the shift is from falciparum malaria to P.vivax malaria. Strategies that have resulted in success against P.falciparum malaria not may be equally applicable to P.vivax malaria, for which elimination of hypnozoites is required. A significant problem in controlling P.vivax malaria is that limitations imposed by Primaquine, the only drug available for eradication of the liver phase of the parasite, prevent many areas from using the drug because of safety concerns[15].

A rapid, inexpensive test for G6PD deficiency that can be used in the field, thus enabling more widespread use of PQ, will be critical to eradication of P.vivax malaria in Pakistan. The test used in the current study is inexpensive which requires a finger prick and can

give result in 10 minutes. This simple procedure with minimal equipment requirements make it useful test for situations in which prompt diagnosis of G6PD deficiency is vital for safe treatment of malaria. Considering the operational challenges more focused approach is required to make this small scale pilot a success when implemented at a large scale.

10 RECOMMENDATIONS

The key recommendation deduced from the pilot activity are as follows

1. Proper criteria for the training nominees should be defined having a specific level of education and experience to conduct the G6PD tests. Only one day training on building the skills of the focal persons for G6PD deficiency screening is not enough and the duration should be increased to at least 3 days for training. This would help in better skills building of the focal persons for G6PD screening. In addition, proper supervision and field testing should also be carried out where trainees field test under supervision of the trainer so that they can identify and report the result properly.

2. A quality assurance mechanism needs to be set in before commencing this type of study. The issues faced by the field teams should have been resolved on spot and the issues identified with RDT kits should have also been resolved on spot. So that quality data could have been gathered for reporting the results.

3. Appropriate logistic plan needs to be set up with timelines for implementation of the study. The logistics should cater proper transport and storage of the kits.

4. The kits should have at least an expiry of 6 months. As the kits were being expired within three months, there were issues in prior planning of the activity, support from the provinces and involvement of the teams.

5. SoPs should be developed for storage, temperature requirement, and utilization of the kits and should be shared with the provincial teams. In case where the kits have to be cross checked a proper mechanism should be described so that all the reported G6PD kits are timely transported for cross checking.

ANNEXURES

ANNEXURE 1: DATA RECORDING FORM

Data Entry Form G6PD Testing of Vivax Positive patients for Radical Treatment											
Province				**District**					**Tehsil/UC**		
Name of Health facility with DHIS Code									**Date of visit**		
Name of patient				**Address**							
Age in years											
Sex	**Male**	**Female**	**TG**								
Ethnic group (✓)	Pashtoons	Baloch	Sindhi	Punjabi	Other	**Sub-cost**					
Marital Status (✓)	Married		Un married	**Children(✓)**	Male	Female----------					
Main presenting complaints (✓)	Fever	Head ache	nausea	vomiting	General body weakness	Other----------					
Microscopy Result (Parasitaemia stage)											
Result of G6PD RDT	Normal Activity		Deficient		Negative Invalid						
Treatment prescribed											
Dates of follow up											
History of Past Illness											

Any history of past malaria attack and history of antimalarial intake including PQ (Yes/No)	
Any drug reaction jaundice, bleeding and hematuria (Yes/No)	
History of marriages in the blood relatives in other ethnic group (as mother , grandmother, from other ethnic group) (Yes/No)	
Any congenital anomaly (cleft lip palate) (Yes/No)	
History of any blood related disorder as Thalassemia, Sickle cell anaemia etc) (Yes/No)	
Any history of drug reaction (Yes/No)	
Any history of blood related disorders in children (Yes/No)	

Any additional remark	**Name & Signature (focal point)**

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