تجمع جازان الصحي
Jazan Health Cluster

DONOR MALARIA TESTING;

CHALLENGES AND OPPORTUNITIES

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Disclosure Statement

I make the following declaration in relation to this CPD Activity :

- This complies with the Ministry of Public Health in Qatar Department of Healthcare Professions MoPH-DHP accreditation standards.
- There is NO Conflict of Interest.
- There is no plagiarism or copyright infringement.
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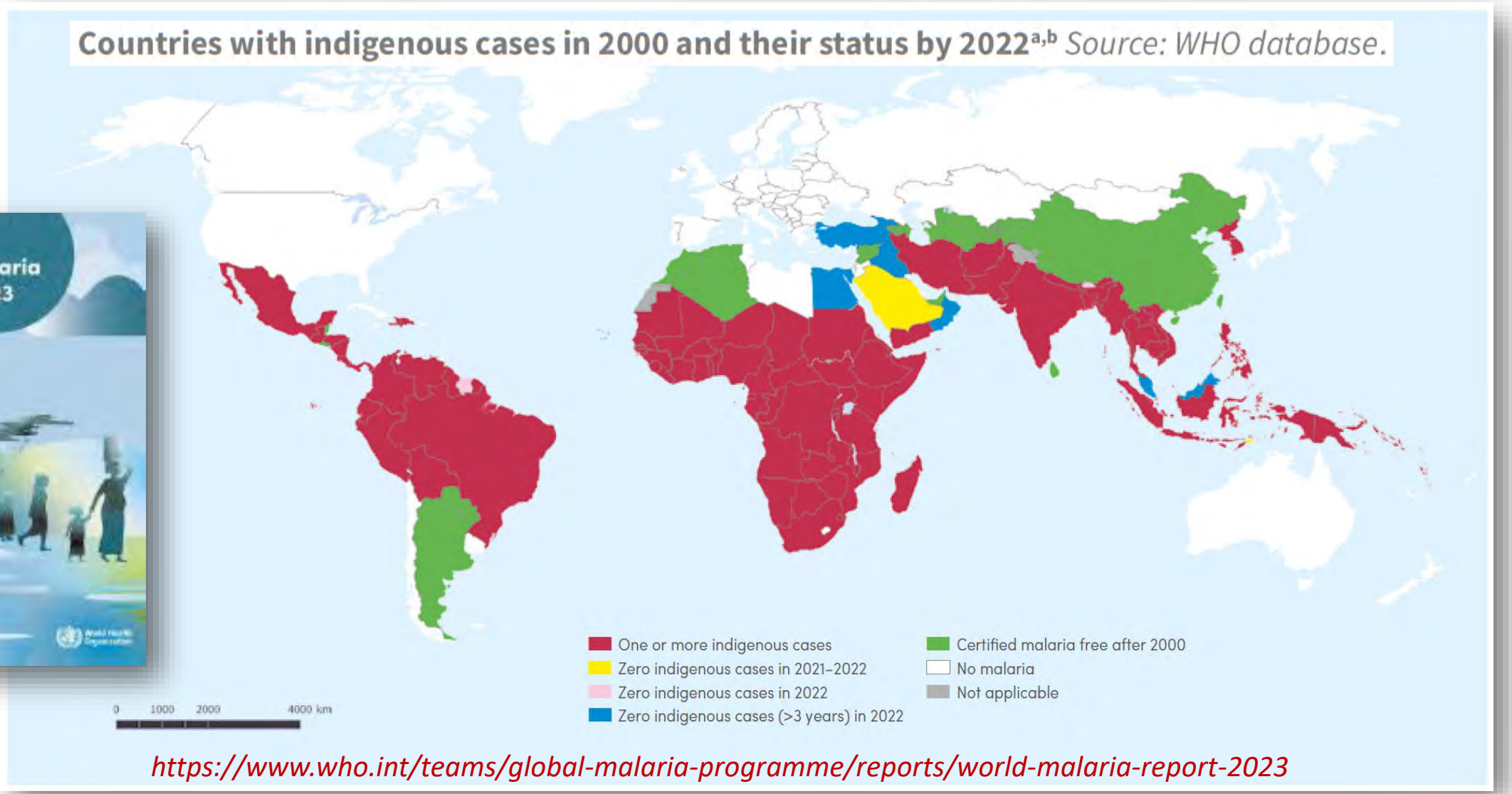
Objectives

- Provide an overview of the global burden of malaria
- Discuss malaria as a transfusion-transmitted disease and current preventive measures in place.
- Discuss currently available diagnostic laboratory tests for malaria and their use for donor testing
- Discuss the factors to consider when testing blood donors for malaria

Epidemiology of Malaria worldwide

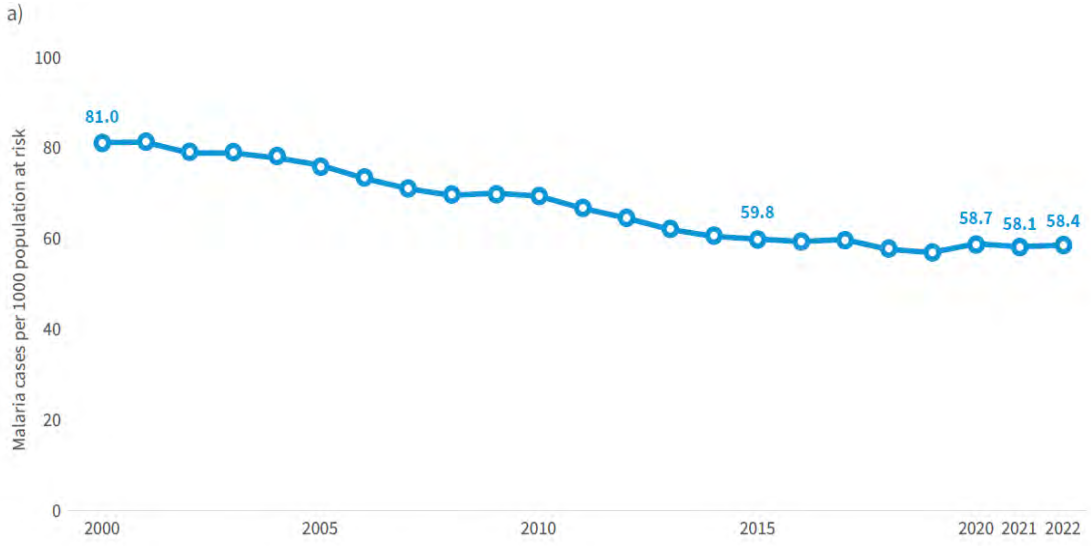


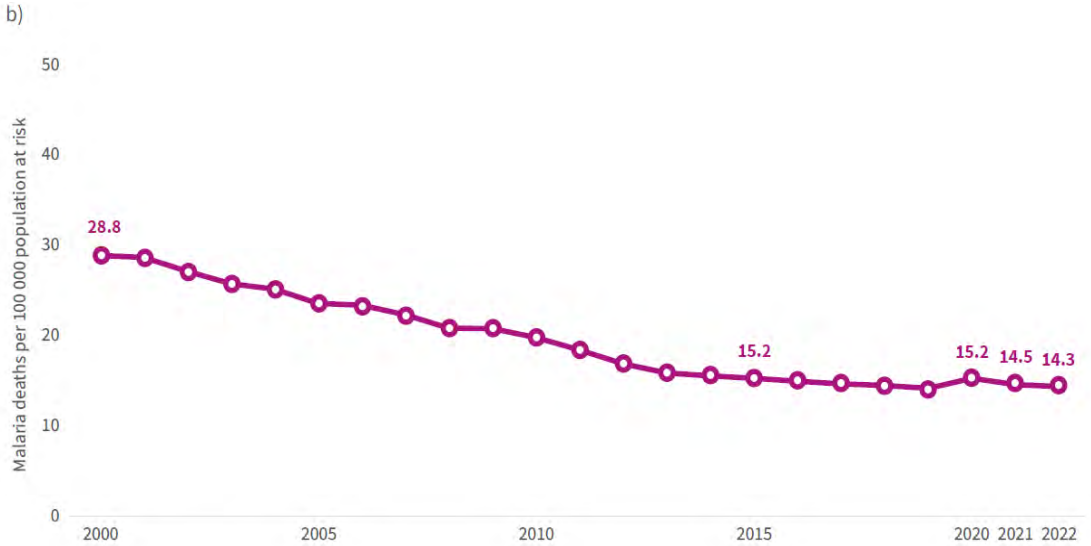
https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2023

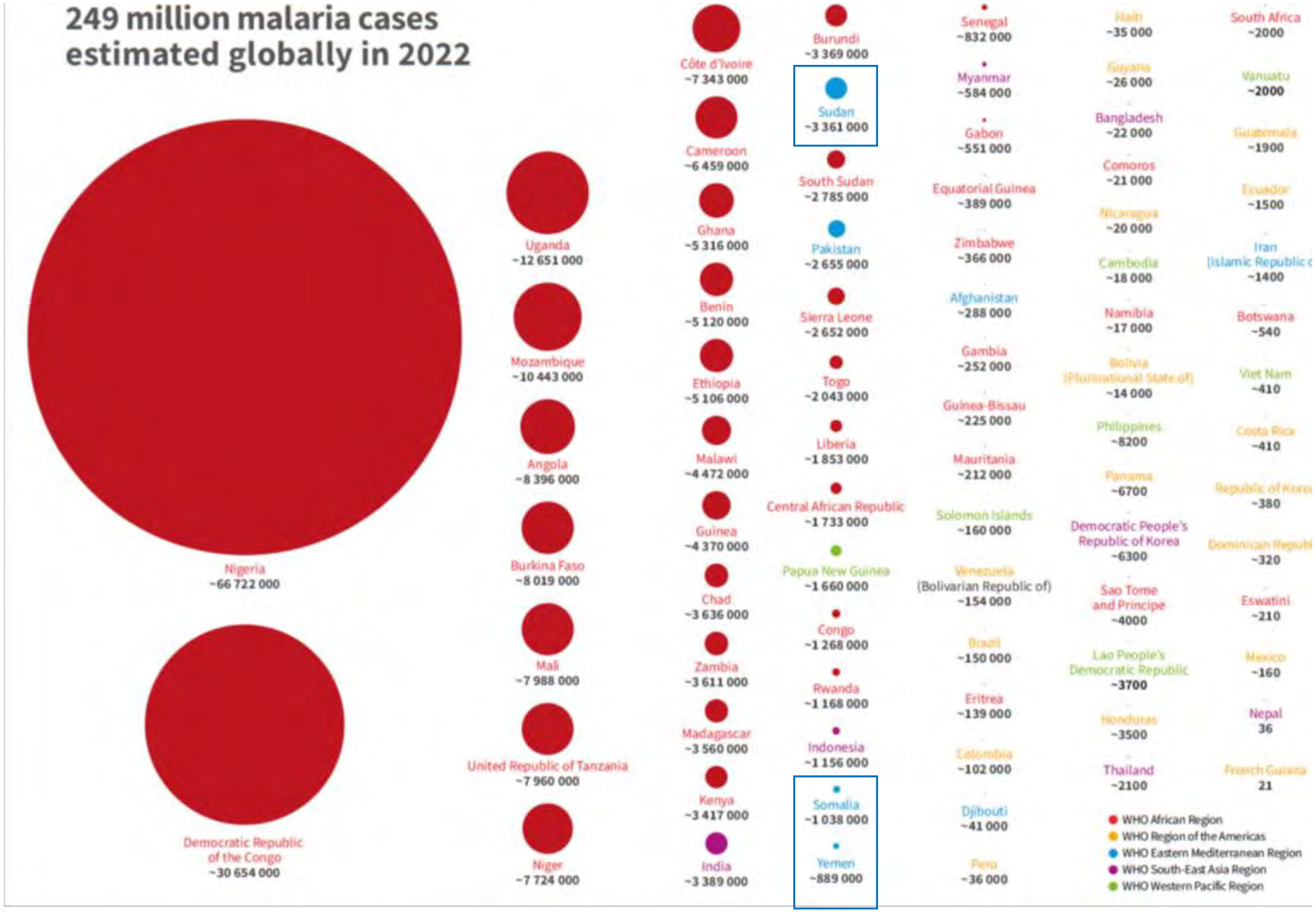
Epidemiology of Malaria worldwide

Global trends in a) malaria case incidence (cases per 1000 population at risk) and b) mortality rate (deaths per 100 000 population at risk), 2000–2022; and c) distribution of malaria cases and d) deaths by country, 2022

Source: WHO estimates. *https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2023*







https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2023

Malaria Causative agents

- Malaria is caused by one or more of the five species of the genus Plasmodium
  - *P. falciparum*
  - *P. vivax*
  - *P. ovale*
  - *P. malariae*
  - *P. knowlesi.*

- These protozoa are transmitted to humans by:
  - The bite of an infected female mosquito of the genus Anopheles.
  - Blood transfusion and organ transplantation
  - Sharing of intravenous drugs or needles.
  - Congenitally

Transfusion-Transmitted Malaria (TTM)

- Transfusion-transmitted malaria (TTM) is rare but serious complication of blood transfusion.
- Asymptomatic blood donors who are infected with malaria parasites can transmit the disease to blood recipients.
- TTM can occur with administration of only a small number of infected donor red cells (10 parasite per unit)*.

* Lazner, E., & Newhouser, E. (1943). Studies on the transmission of malaria by blood transfusions. Am J Med Sci, 204, 141-146.

Transfusion-Transmitted Malaria (TTM)

- Worldwide, around 3,000 cases of TTM were reported between 1950 and 1980.
- Estimates of the frequency of post-transfusion malaria vary from less than 0.2 cases per million units of blood transfused in non-endemic countries to 50 or more cases per million in some endemic countries.
- In the USA, 98 cases were reported between 1963-2009, and in UK 5 cases were documented between 1986-2006
- In Arab countries, TTM is not known due to poor reporting.

TTM risk-reduction Strategies

- Strategies to reduce TTM differ between countries based on the incidence of malaria (Endemic vs non-endemic countries/areas).

Donor screening	Donor deferral based on previous infection, residency, or travel history
Donation screening	Laboratory testing of donor's blood specimen for malarial markers
Product modification	Pathogen inactivation
Recipient care	Differential diagnosis, recipients' education, and drug prophylaxis

Current challenges with TTM

- Lack of reporting (haemovigilance programmes)
- Re-emerging malaria
  - Iran: 2022
  - USA: 2023
- Various donor deferral policies across the globe
  - Donor lost
  - Donor deferral due travel
  - blood availability (rare donors)
  - blood safety (parasitaemia persistence in asymptomatic donors)
- Donor vs. donation screening
  - Safety of current deferral policies
  - No standardised lab testing method

How effective is the donor deferral in preventing TTM?

Transfusion-transmitted malaria not preventable by current blood donor screening guidelines: a case report

THE JOURNAL OF AABB TRANSFUSION transfusion.org

Holtzclaw, Arthur, et al. *Transfusion* 56.9 (2016)

- A 76-year-old male presented with UTI.
- admitted to ICU and initiated on broad-spectrum antibiotics.
- On Hospital Day 2, intraerythrocytic parasites on PS, identified as *P. malariae* by PCR
- No recent foreign travel or exposure to malaria
- Received 15 RBCs in the past 6 years.
- Index samples from the 10 most recent units obtained, one tested positive for *P. malariae* via serology.
- The donor was a 20-year-old male who immigrated to USA from Liberia at the age of 5 with no subsequent travel or exposure to malaria.

Methods for malaria parasite detection and diagnosis

- CONVENTIONAL METHODS
  - Light microscopy
  - Immunochromatography-based rapid diagnostic test (RDT)
- DE VELOPED ME THODS
  - Enzyme-linked immunosorbent assay (ELISA)
  - Flow cytometry

- ADVANCED MOLECUL AR TECHNIQUE
  - Real-time PCR
  - Multiplex PCR
  - Nested PCR
  - Loop-mediated isothermal amplification (LAMP)
  - Recombinase polymerase amplification
  - Molecular-based POCT
  - Other advanced molecular techniques
    - droplet digital PCR (ddPCR) and next generation sequencing (NGS)

Methods for malaria detection in blood donors

1. Direct parasite demonstration

- Conventional microscopy
  - Thick & thin films stained with Giemsa, Field, or Wright stains
  - 5-100 parasite /ul, but in most labs is 500 /ul
  - Has several disadvantages

- CELLSCHECK system
  - Rapid automaton platform for detection and identification Plasmodium species in human blood by the thick drop method.
  - LoD 50-150 parasite /ul.
  - Has Specificity issues

Methods for malaria detection in blood donors

2. Parasite-derived antigen detection

- RDT (immunochromatographic) malarial antigen assays based on detection of:
  - histidine-rich protein 2 (pHRP-2
  - plasmodial lactate dehydrogenase (pLDH)
  - 100-1000 parasite/ul

- Antigen EIA.
  - histidine-rich protein 2 (HRP2)-based ELISA
  - Detects only for *P. falciparum*
  - As low as 1 parasite/ul

Methods for malaria detection in blood donors

3. Indirect parasite detection

- Antibody-based EIA
  - About 65-95% specificity
  - Not suitable for endemic areas

4. NAT (PCR/TMA)

- PCR
  - USA FDA recently approved Cobas Malaria assay on Cobas 6800/8800 systems
- TAM
  - Saudi MOH currently validates a new molecular assay (Procleix Plasmodium Assay)
- Highly sensitive (as low as 0.004 parasite /ul)

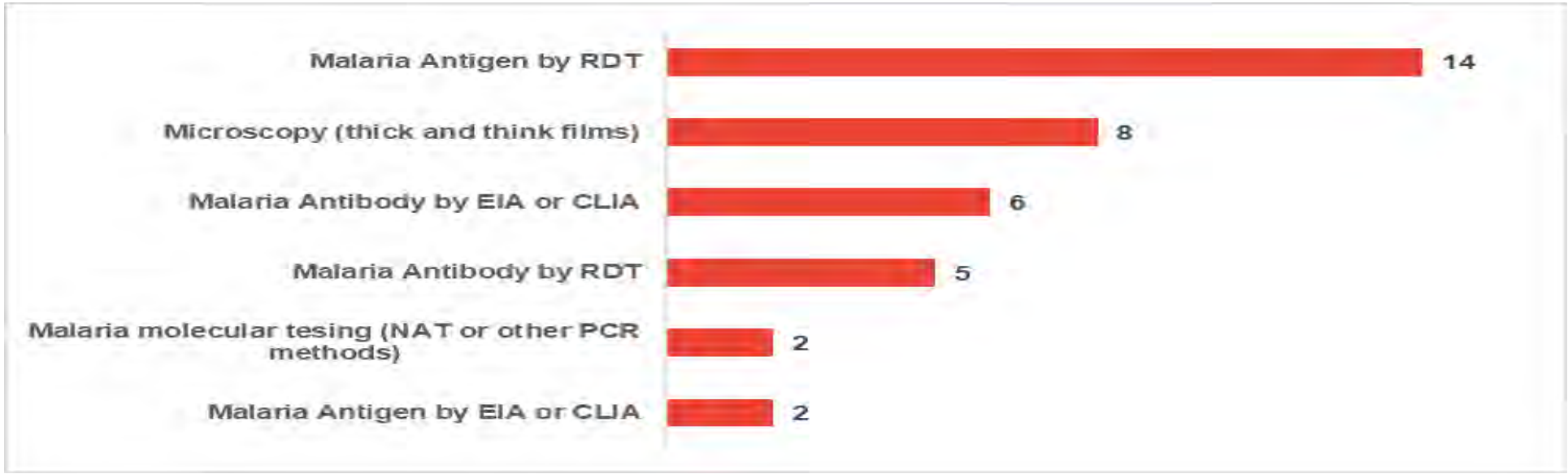
Donor Malaria testing in Nonendemic Regions

Country	Assays used
France	ELISA Malaria Ab (Diapro) 1th line ELISA Anti-Plasmodium (IgG) (Euroimmun) 2nd line
Portugal	Malaria EIA (Bio-Rad)
Greece	NovaLisa™ Malaria Elisa (NOVATEL Immundiagnostics GmbH)
Italy	Different assays
Netherland	Captia™ Malaria Total Antibody EIA (Trinity Biotech)
Switzerland	Anti-Plasmodium (IgG) (Euroimmun), Malaria EIA (Bio-Rad)
UK	Captia Malaria Total Ab EIA (Trinity Biotech)

Adopted from:
Niederhauser, C., & Galel, S. A. (2022). Transfusion medicine and hemotherapy, 49(4), 205-217.

Transfusion-Transmitted Malaria and Mitigation Strategies in Arab countries*

- 28 responses from 12 Arab countries
- Donor malaria testing is nationally required in 50% of the responding countries
- Ag-RDT is the most used method



* Personal communication (short electronic survey conducted Nov'24)

Which malarial test is most reliable and appropriate for donor testing?

Electronic Physician (ISSN: 2008-5842) http://www.ephysician.ir

February 2016, Volume: 8, Issue: 2, Pages: 2001-2005, DOI: http://dx.doi.org/10.19082/2001

Blood donors screening for malaria in non-endemic area in the Kingdom of Saudi Arabia: Is it necessary to introduce immunological testing?

Ghaleb Elyamany[1,2], Ali Al Gharawi[1], Mohammed Alrasheed[1], Omar Alsuhaibani[1]

[1] Department of Central Military Laboratory and Blood Bank, Prince Sultan Military Medical City, Riyadh, Saudi Arabia

[2] Department of Hematology, Theodor Bilharz Research Institute, Egypt

- 180,000 Saudi (87%) and non-Saudi (13%) blood donors tested by microscopy.
- None (0%) was found positive

Which malarial test is most reliable and appropriate for donor testing?

Parasitol Res (2011) 108:1519–1523
DOI 10.1007/s00436-010-2207-1

ORIGINAL PAPER

Detection of malaria infection in blood transfusion: a comparative study among real-time PCR, rapid diagnostic test and microscopy

Sensitivity of Malaria detection methods in blood transfusion

Gholamreza Hassanpour · Mehdi Mohebali · Ahmad Raeisi · Hassan Abolghasemi · Hojjat Zeraati · Mohsen Alipour · Ebrahim Azizi · Hossein Keshavarz

- 100 Iranian blood donors selected from endemic and malaria-free areas tested by microscopy, RDT, and RT-PCR methods
- 2/50 (4%) were positive (from the endemic area) only by RT-PCR

Which malarial test is most reliable and appropriate for donor testing?

OPEN ACCESS
The Journal of Advances in Parasitology
Research Article
April 2015 | Volume 2 | Issue 2 | Page 40

Detection of Malaria in Healthy Blood Donors using PCR in an Endemic Area in Yemen

RAGAA ALI OTHMAN[1*], HANAN ELSAYED ELDEEK[1], AMAL MOHAMMED ALMATARY[1], AYAT ABDELRAHMAN SAYED[2], ASMAA ALSAKAF[3]

[1]Department of Parasitology; [2]Department of Biochemistry, Faculty of Medicine, Assiut University, Egypt; [3]Department of Parasitology, Faculty of Medicine, Ministry of Health, Yemen.

- 200 Yemeni blood donors tested by microscopy and nested PCR methods
- 33/200 (16.5%) were positive by PCR
- 28/200 (14%) were microscopically positive

Results	Microscopic examination (n=200)		PCR (n=200)	
	No.	%	No.	%
Positive cases				
P. Falciparum	26	13	33	16.5
P. Vivax	2	1	0	0
Mixed	0	0	0	0
Negative cases	172	86	167	83.5

Which malarial test is most reliable and appropriate for donor testing?

- 1500 Ghanaian blood donors tested by microscopy, RDT, and nested PCR methods

Malaria Research and Treatment

Research Article | Open Access

The Incidence of Malaria Parasites in Screened Donor Blood for Transfusion

Samuel Antwi-Baffour, Ransford Kyeremeh, Atta Poku Amoako, Lawrence Annison, John Ocquaye-Mensah Tetteh, Mahmood Abdulai Seidu

First published: 25 November 2019 | https://doi.org/10.1155/2019/1457406 | Citations: 6

Table 1: Age ranges and gender of donors against percentage of malaria positive slides.

Age ranges	Frequency *N* (%)	Microscopy test–positive (%)	Rapid diagnostic test–positive (%)	Molecular test–positive (%)
20–29	495 (33)	24	25	24
30–39	645 (43)	6	6	6
40–49	300 (20)	15	15	14
50–59	60 (4)	3	3	3
Total	1,500	48	49	47
Gender				
Male	1,215 (81)	39	40	39
Female	285 (19)	9	9	8
Total	1,500	48	49	47

Which malarial test is most reliable and appropriate for donor testing?

Basic Medical Research

Evaluating laboratory screening tests for malaria on blood donor candidates to reduce the risk of transfusion-transmitted malaria in an endemic area of Indonesia

Nethasia Louhenapessy,[1] Ria Syafitri Evi Gantini,[1,2,3] Susan Rahayu,[4] Elisabeth Lilipory,[5] Heri Wibowo,[6] Yuyun Soedarmono,[7] Inge Sutanto[6]

Louhenapessy, Nethasia, et al. Medical Journal of Indonesia 30.3 (2021): 191-7.

- 248 Indonesian blood donors tested for 18S rRNA gene by PCR
- 3/248 (1.2%) were positive by PCR
- 22/550 (4%) were positive by rapid antibody test

Table 1. Malaria positive rate based on various laboratory tests

Time period	N	Microscopic (Giemsa staining)	Rapid antigen (Pf-HRP2 and Pv-LDH)	Rapid antigen (Pf-HRP2-pan aldolase)	Rapid antibody (α-MSP-Pf Pv)	PCR 18S rRNA
First term	302	0	0	0	6.3% Pf (19)	Not done
Second term	248	0	0	0	1.2% Pf (3)*	1.2% (3)†
Total	550	0	0	0	4% Pf (22)	0.5% (3)

Donor malaria NAT Testing, to test or not to test?

Use of a NAT-based assay to improve the surveillance system and prevent transfusion-transmitted malaria in blood banks

Rocha, Daniele, et al. Malaria Journal 19 (2020): 1-9.

- 4745 eligible donors in western Brazilian Amazon tested with multiplex NAT for S18 rRNA gene
- 3 (0.06%) were positive
- NAT assay was effective in detecting infected candidate donors and has good prospects to be applied in routine screening for preventing TTM'.

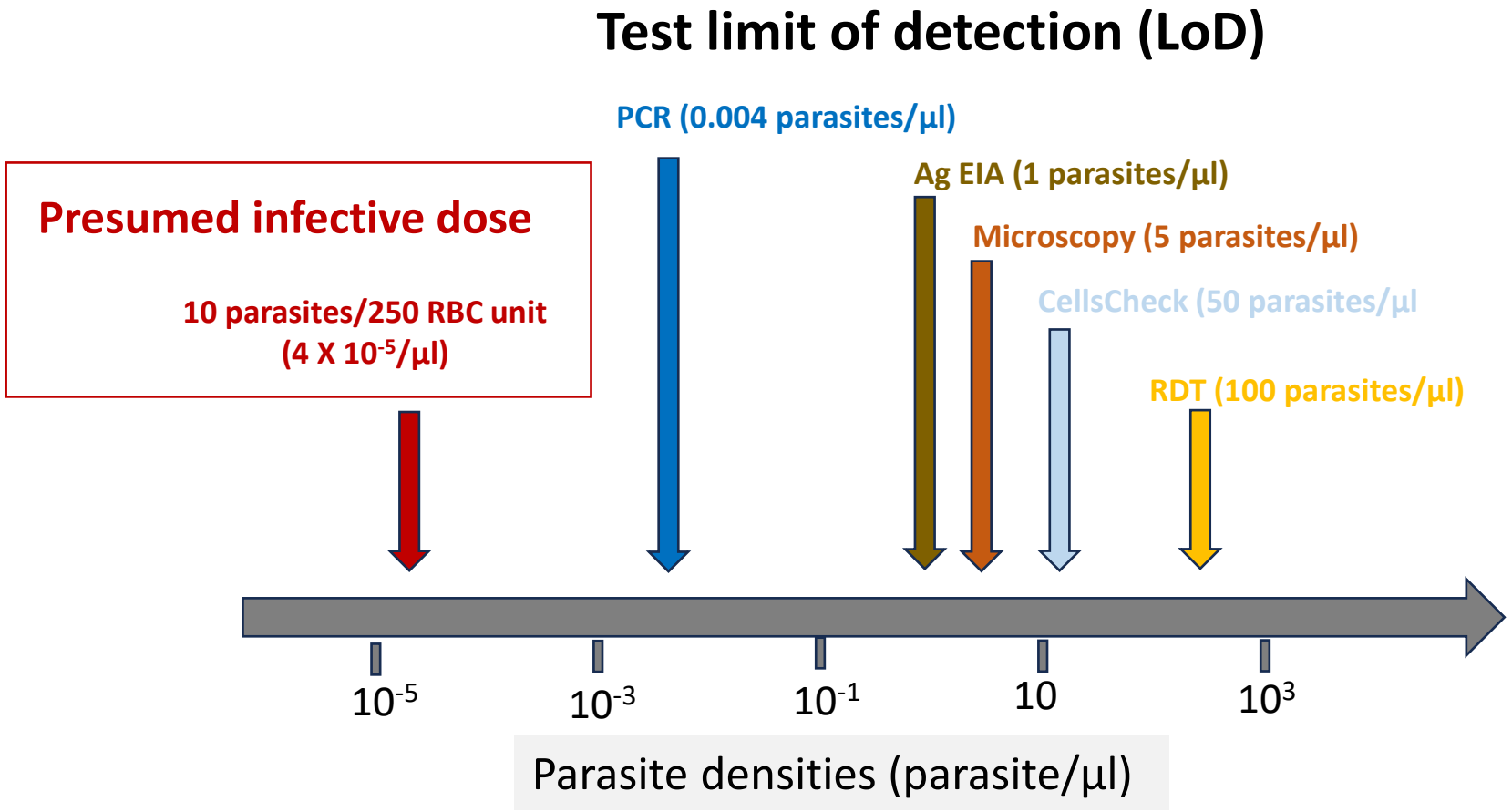
J Haematol Stem Cell Res. 2021; 1(2): 98-101 Original Article

Molecular Screening for Malaria Parasitemia among Blood Donors: A Regional Transfusion Center Study in Pakistan

Mohammad Abdul Naeem[1]
Muhammad Ali Rathore[2]
Anum Javed[3]
Mansoor Ishaq Raja[4]
Maria Khan[5]

- 1000 asymptomatic donors tested for S18 rRNA subunit by RT-PCR
- Only 1 (0.1%) was positive
- Malaria appears to be very uncommon in asymptomatic male blood donors and screening by NAT would not be economical

Which test should be used to screen blood donors for malaria?



Require 100-fold sensitive NAT to detect every infective donors

Adopted from:

Seed, Clive R., Alan Kitchen, and Timothy ME Davis. Transfusion Medicine Reviews 19.3 (2005): 229-240.

Factors to consider when testing blood donor for malaria

- Epidemiology
  - Endemic vs non-endemic area
  - Risk-assessment
  - Surveillance
- Regulations
  - Donor deferral
  - Donor re-entry
  - Testing methods
- Cost analysis

- Testing approach
  - Testing method
  - All vs. selective testing
  - NAT ID v. MP testing
  - Testing vs pathogen reduction
- Donor care
  - Education
  - Counselling
  - Lookback

I summary…

- TTM is a very rare complication of blood transfusion.
- The magnitude of TTM in Arab countries is not known.
- No single malaria test that can prevent 100% of TTM.
- Adopt a systematic approach to implement a new donor malaria test or to assess efficiency of current one.
- Continuous risk assessment of TTM for a better donor deferral and testing strategies.


THANK
YOU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