Insecticide resistance in malaria vectors: latest updates from IR Mapper®

Melinda P. Hadi[1], Elijah O. Juma[1], Helen Pates Jamet[2]

[1]Vestergaard Frandsen (EA) Ltd, Nairobi, Kenya

[2]Vestergaard Frandsen Inc, 1020 19th St NW, Washington DC, 20036, USA

Introduction

Rational decision making on insecticide resistance management requires detailed knowledge of both the spatial distribution of resistance and the resistance mechanisms involved. In addition to phenotypic data on resistance obtained through conducting susceptibility tests using the WHO susceptibility test and/or CDC bottle assays, data on resistance mechanisms is also essential. In particular, data on metabolic-based resistance are required as there is increasing evidence that metabolic mechanisms play a more significant role than target-site resistance in conferring resistant phenotypes (WHO, 2012).

IR mapper® (www.irmapper.com) was launched in 2012 and is an online geospatial platform for mapping insecticide resistance in malaria vectors, built on a systematic review of peer-reviewed, published literature. The user interface enables filtering of vector species, insecticide class and type, and resistance mechanisms data including target-site mutations relevant for current public health insecticides (*kdr* (L1014S, L1014F) and *ace-1*^{R}), and metabolic mechanisms related to enhanced activity of esterases, cytochrome P450 monooxygenases, GSTs (glutathione s-transferases), and PGP (P-glycoprotein) efflux pump.
Based on user-directed filtering criteria, IR Mapper® generates an overview of the insecticide resistance data available and also identify the data gaps

Methodology

Data extracted from peer reviewed scientific publications on insecticide resistance are available on IR Mapper® (www.irmapper.com). Additional unpublished data derived from standard WHO susceptibility tests and CDC bottle bioassays from President's Malaria Initiative, National Malaria Control Programmes, and other reputable institutions were also included.

Methods to determine insecticide resistance (phenotypic data):	Methods to determine resistance mechanisms:
• WHO susceptibility test • CDC bottle assay	• Molecular testing (PCR, qPCR) • Microarray • Biochemical assay • Synergist assay

The filter tools on IR Mapper® enables filtering by year, vector species, insecticide class, and resistance mechanisms. For instance, filtering by time periods produces maps that convey the change in the status of insecticide resistance (Figure 1). Filtering by resistance mechanisms also highlights the areas where available data concentrate (Figure 2).

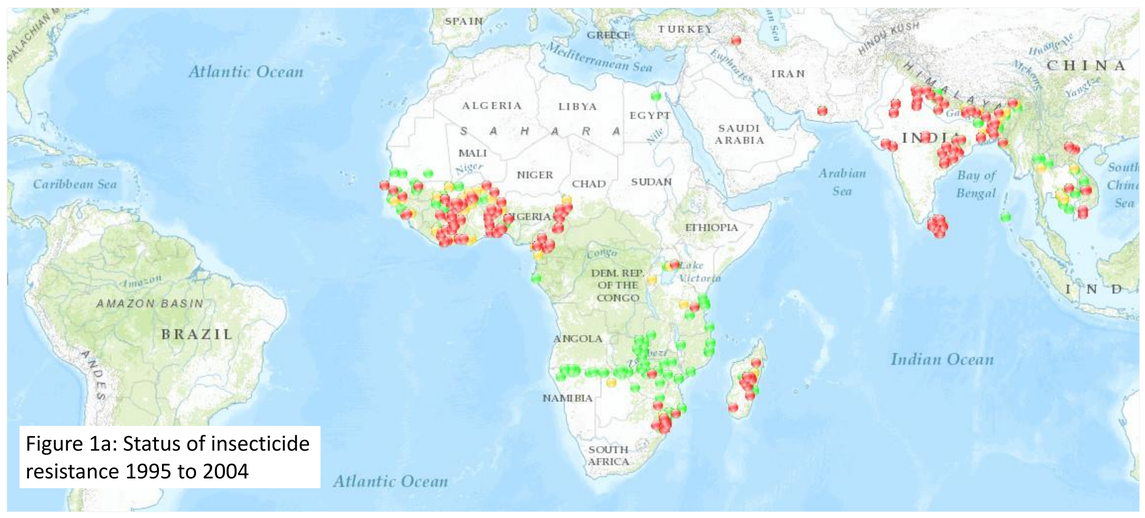

Figure 1a: Status of insecticide resistance 1995 to 2004

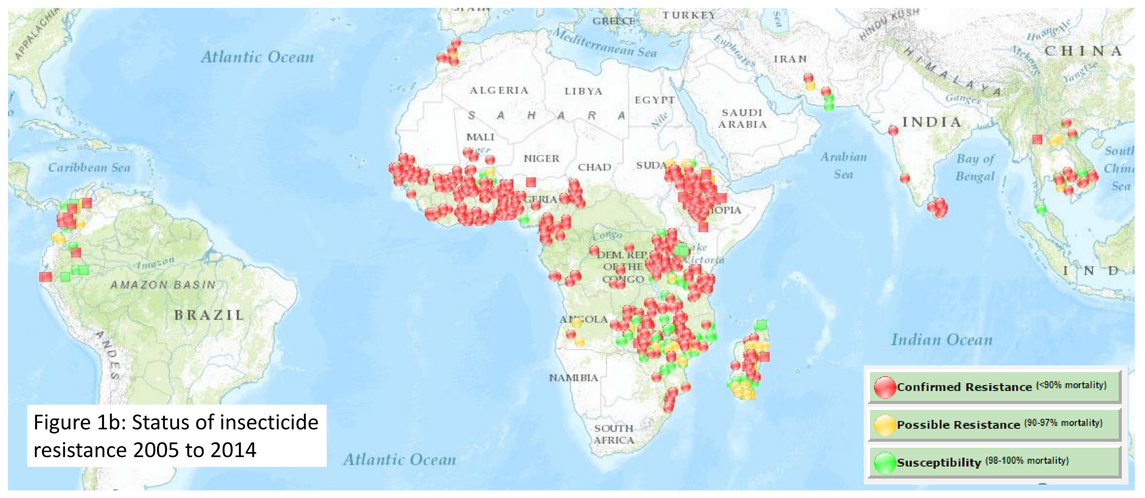

Figure 1b: Status of insecticide resistance 2005 to 2014

(Source: www.irmapper.com)

Figure 1a & b. Screenshots of IR Mapper® with available data on insecticide resistance from 1995 to 2004 and 2005 to 2014

Results

Target site and metabolic resistance mechanisms data on IR Mapper®

Figure 2a: Target site resistance mechanisms (1995 to 2004)

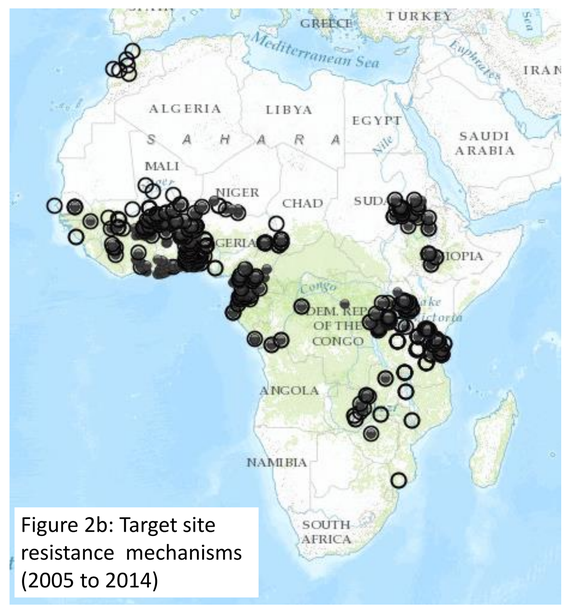

Figure 2b: Target site resistance mechanisms (2005 to 2014)

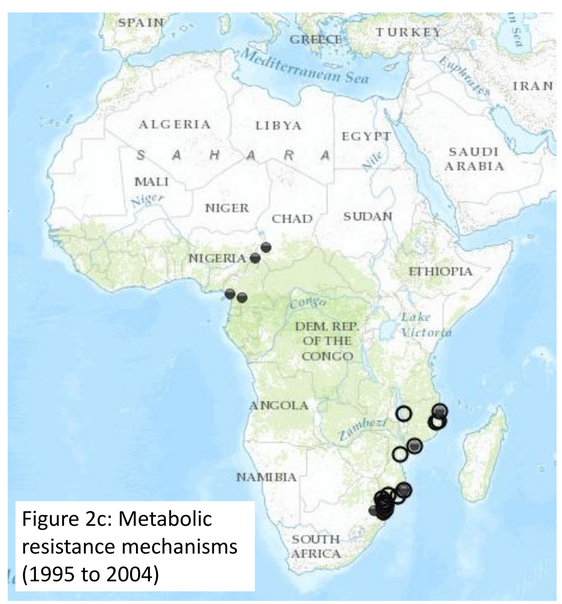

Figure 2c: Metabolic resistance mechanisms (1995 to 2004)

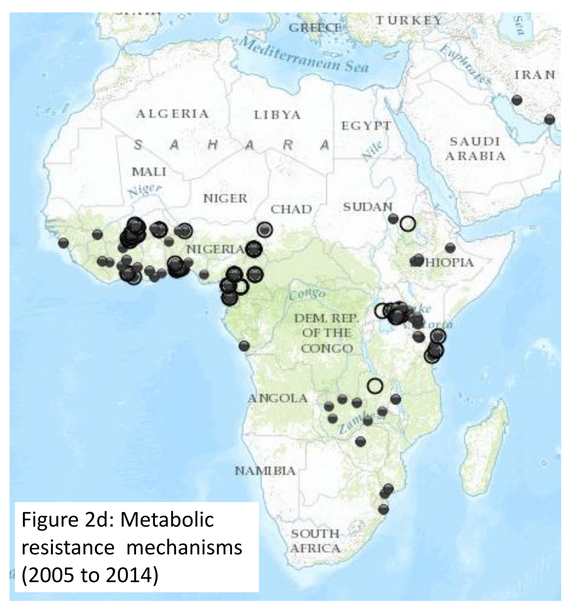

Figure 2d: Metabolic resistance mechanisms (2005 to 2014)

(Source: www.irmapper.com)

Figure 2 (a to d): Target site resistance (*kdr* (L1014S, L1014F) and *ace-1*^{R} mutations) and metabolic resistance (esterases, cytochrome P450 monooxygenases, GSTs, PGP pumps) in *Anopheles* species from 1995 to 2004 and 2005 to 2014. (● detected; ○ not detected)

- An IR Mapper® search including publications from 1954 up to 2014 yielded 57 countries with confirmed insecticide resistance and documented resistance mechanisms. There was a marked increase in insecticide resistance testing in the 10 year period from 2005 to 2014, compared to the previous decade from 1995 to 2004 (Figure 1a & b)
- Increased testing and reporting of target site mechanisms (Figure 2a & b) and metabolic mechanisms (Figure 2c & d) were also observed in the last decade
- Of the 1351 reports of resistance mechanisms testing in the Afrotropical region, 75% were target site assays and 25% metabolic mechanisms assays. Even where metabolic testing was conducted, it continues to be reported only in a limited number of countries (Figure 2d)
- Notably, metabolic resistance data are particularly lacking in two countries of high malaria burden: Nigeria and Democratic Republic of Congo.

Conclusion

The IR Mapper® application is a useful tool for visualising the status of insecticide resistance and associated target site and metabolic resistance mechanisms. In the ten year period from 2005 to 2014, more susceptibility testing was conducted, and more sites and areas of resistance were detected than in the previous decade. Target site mutations are more frequently tested at sites of confirmed resistance, though an increase in reported metabolic resistance was observed.

IR Mapper® is also able to identify key areas where data gaps on insecticide resistance exist in malaria vectors. At present, resistance mechanism data are particularly lacking in high malaria burden countries such as Nigeria and Democratic Republic of Congo. While countries are increasingly conducting susceptibility testing as part of routine insecticide resistance monitoring, characterising target site and metabolic mechanisms must be encouraged for a complete analysis of the resistance situation in order to guide rational decision making in vector control programmes.

IR Mapper

For more information, please contact Elijah Juma (eoj@irmapper.com)

esri Eastern Africa

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