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# Pilot assessment of point-of-care differential white blood cell counts in school children with schistosomiasis

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## Abstract

Public health monitoring of schistosomiasis needs appropriate field-based technology, so to expand this portfolio, we conducted a first pilot assessment of point-of-care differential white blood cell count analysers. In total, 120 Malawian primary school children were examined with  
15 six key haematological parameters recorded. A notable proportion had abnormal differential white blood cell profiles with eosinophilia (48.3%) positively associated with schistosomiasis (OR 3.2, 95% CI 1.3-7.7). Whilst costs of equipment and associated tests were non-trivial, both machine performance and haematological information gained were satisfactory. To improve  
20 monitoring of schistosomiasis-associated pathologies, inclusion of differential white blood cell count technology screening appears sensible.

## Keywords

Surveillance, haematology, eosinophilia, urogenital schistosomiasis, intestinal schistosomiasis, sub-Saharan Africa.

## Introduction

25 Schistosomiasis is a major public health challenge across much of sub-Saharan Africa (SSA), despite the implementation of preventive chemotherapy control campaigns that reduce population morbidity and onward schistosome transmission [1]. Regular monitoring of sentinel at-risk populations is essential to determine the health impact of current interventions, but contemporary public health surveillance does not include differential white blood cell (dWBC)

30 analysis, as appropriate point-of-care (POC) technology is lacking. This deficit in assessment is clearly at odds with measurement of eosinophilia, for example, in routine use for clinical assessment where haematological services are locally available [2].

Since 2021, the HemoCue® WBC DIFF System became commercially available in the United Kingdom. Using fingerprick blood and specialist microcuvettes with lyophilised reagents, 35 this light weight and portable analyser provides a total WBC count with differential cell counts for neutrophils, lymphocytes, monocytes, eosinophils and basophils, respectively. Only minimal assay training is needed, over and above standard POC protocols, for example, those in common use for the HemoCue® Hb 801 analyser, a ‘field-standard’ for measurement of haemoglobin levels. In our opinion, the HemoCue® WBC DIFF System could be used to provide 40 a novel field-based solution for better haematological assessments, augmenting POC measurements of haemoglobin, improving public health documentation of schistosomiasis-associated pathologies.

Our intention here was to share our field experiences, machine performance and data interpretation concerning first pilot assessment of POC dWBC technology for field monitoring of 45 schistosomiasis within school-aged children. Our primary school setting in Malawi is typical of much of SSA elsewhere, where local infrastructure, e.g. on-site electricity, is limited and standard parasitological diagnostics for epidemiological surveillance of schistosomiasis were used.

## Methods

50 As part of the HUGS (Hybridisation in UroGenital Schistosomiasis) investigation (see [www.lstmed.ac.uk/hugs](http://www.lstmed.ac.uk/hugs)), a pilot epidemiological survey was undertaken in November 2022, visiting two primary schools (Samama [14.417465° E, 35.217580° S] and Mchoka [14.439481° E, 35.220644° S]), where both urogenital schistosomiasis (UGS) and intestinal schistosomiasis (IS) were previously documented [3].

55 Standard parasitological surveillance methods were used in this current pilot survey for UGS by urine filtration (10 ml) and for IS with urine-circulating cathodic antigen (CCA) dipsticks, see [3]. Using a lancet and an appropriate HemoCue® microcuvette, fingerprick blood was collected, with Hb (g/l) and dWBC (Total WBC x10<sup>9</sup>/l) and neutrophils, lymphocytes, monocytes,

eosinophils, basophils  $\times 10^9/l$  and %) measured with a HemoCue<sup>®</sup> Hb 801 analyser and a  
60 HemoCue<sup>®</sup> WBC DIFF analyser, respectively (Radiometer UK Limited, Crawley, UK).

*<please insert Figure 1 near here>*

In the field, we noted that the HemoCue<sup>®</sup> WBC DIFF analyser was sensitive to vibration, needing placement on a solid stand-alone table with shielding from direct sunlight and dust, and required a stable external power supply, Figure 1A. If so managed, and using two machines  
65 in parallel, rapid POC examination of school children was achieved with dWBC results available within five minutes. On each day of operation, a spot-quality control of five different fingerpick blood samples, analysed in duplicate, was spot-checked. Any dWBC tests that did not report upon first attempt were repeated, with the Invalid Test Rate (ITR), the proportion of failed tests, were noted specifically.

70 Upon subsequent data validation and curation, a complete dataset of urine-egg counts, urine-CCA dipsticks, Hb and dWBC was available from 120 school-aged children (mean age 10 years 11 months, male [53.3%] and female [46.7%]), a pragmatic sample size typical of school-based surveillance for schistosomiasis in disease mapping [1]. Cross-tabulations, with essential statistical analyses, were undertaken in R\_Studio (version 4.1.3) with graphical outputs  
75 using ggplot2, from the tidyverse package (<https://ggplot2.tidyverse.org/>).

## Results

Urine-egg patent prevalence of UGS was 59.1% while urine-CCA dipstick prevalence of IS was 43.3%, considering trace results as positive. Co-infection prevalence of UGS and IS was 29.2%. Under operating conditions, as described above, the ITR of the Hemocue<sup>®</sup> Hb 801 was ~0.5%,  
80 while that of the HemoCue<sup>®</sup> WBC DIFF analyser was ~7.5%. The spot-quality control check revealed no concerning discrepancies between either machine readings.

Box-and-whisker plots, shown in Figure 1B, illustrate the children's schistosomiasis status against: Hb, total WBC count and percentage of neutrophils, lymphocytes, monocytes, eosinophils and basophils, respectively. Importantly, the majority of total WBC counts fell below  
85 the reference range (65.8%), an often noted trend for participants in SSA when using 'normal' reference ranges obtained from American or European reference standards [2]. Attempting to mitigate this, percentage ranges of dWBC values were used for our statistical analysis, rather

than absolute cell counts. Importantly, the majority of total WBC counts fell below the reference range (65.8%), an often noted trend for participants in SSA when using ‘normal’ reference ranges  
90 obtained from American or European standards [2,4]. Attempting to mitigate this, analysis of the percentage range of dWBC values were used rather than absolute cell counts comparisons. Compared to schistosomiasis-negative children, ‘any’ schistosomiasis was positively and statistically significantly associated (OR 3.2, 95% CI 1.3-7.7) with eosinophilia, defined as eosinophils >3% of total WBC. Co-infection with both UGS and IS was also positively associated  
95 and statistically significant (OR 4.3, 95% CI 1.5-12.1) with eosinophilia, as was single infection with UGS (OR 2.86, 95% CI 1.0-7.9) but IS alone did not show statistical significance (OR 2.3, 95% CI 0.7-7.7).

## Discussion

This pilot assessment has demonstrated the first use of the HemoCue® WBC DIFF system  
100 under field conditions to improve haematological assessment of schistosomiasis in school children from Malawi. We have shared our experiences and guidance for optimum machine functionality within a local environment where grid electrical supply was often unreliable.

Considering the ITR for Hb and dWBC assays and reflecting upon experiences gained in the field, it was found that the internal power supply (three AA batteries) was sufficient alone for  
105 use of the Hemocue® Hb 801. This machine was very robust with results available within less than 15 seconds. However, the internal power supply (six C batteries) for use of the HemoCue® WBC DIFF was unsuitable, requiring an external 12 V Enhanced Flooded Battery (EFB) with DC/AC inverter, Figure 1A. The DC/AC inverter could be used in the evenings of each day to recharge the EFB when grid electricity was available.

In terms of expenses incurred in 2022, the initial purchasing cost of the HemoCue® WBC  
110 DIFF analyser was £3,480, with £3.10 per microcuvette. By comparison, the initial purchasing cost of the HemoCue® Hb 801 analyser was £749, with £0.59 per microcuvette. However, using a single lancet, £0.75 per unit, some cost-sharing across blood collection methods was achieved. Local purchase of the DC/AC inverter and EFB incurred a further £250 and if two dWBC  
115 machines were used in parallel, then the time taken to analyse children’s blood samples did not unduly delay any other ongoing survey activities, with workflows running smoothly.

Of special note here, the ITR for the HemoCue® WBC DIFF system was some fifteen-fold higher than the HemoCue® Hb 801 analyser, which necessitated increased repeat testing of children, raising the total cost per child examined. Compared to the costs of other dWBC laboratory analyses and recommendation time of trained staff required, we consider these costs relatively low and largely affordable. Upon consideration of typical POC surveillance costs, future use of POC dWBC technology could also provide a useful adjunct to more advanced field-based screening methods of schistosomiasis-associated morbidity, e.g. POC ultrasonography, for improved individual or population monitoring. It could be used, for example, to better identify at-risk individuals, populations or communities in further need of closer clinical or epidemiological inspections, as well as, assessment before and after intensified schistosomiasis control.

In addition to the expected positive associations of eosinophilia with schistosomiasis, our results are notable for reduced total WBC counts and neutrophils (both as an absolute count and as a percentage) and increased lymphocyte counts, with most results falling outside the normal reference ranges. This has been noted previously in individuals of African descent [2,5] when using reference values that have traditionally been defined with American- or European-centric standards [4], which might change our first epidemiological appraisal here.

While further exploration of these dWBC profiles is beyond the scope of this paper, an increase in the wider application of POC dWBC screening in SSA could provide better local reference ranges. Using these data, deeper insights into interpretation of abnormal dWBC profiles where schistosomiasis, and other helminthiases are endemic, would be possible. For example, the HUGS study subsequently used this dWBC technology within its longitudinal population study at Samama village where the community was offered preventive chemotherapy annually then biannually. These findings are soon to be reported elsewhere.

## **Conclusion**

Our pilot assessment is the first to use dWBC technology for more detailed POC haematological investigations of schistosomiasis-associated pathologies. While initial investment and per-test costs are higher than basic Hb testing, the added haematological information may justify the expense for targeted surveillance, especially compared to the cost of laboratory WBC analysis. Future use of this technology could improve the portfolio of public health monitoring in regions

lacking formal laboratory facilities and even assist in the development of more appropriate dWBC references value tables in SSA.

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### 155 **Author’s contributions**

**SR** - fieldwork, data collection, data curation, data analyses, manuscript drafting; **JW** - data curation, data analyses, **PM** - fieldwork, project management, **SAK** - fieldwork, clinical oversight, **JM** - fieldwork, project management, **JRS** - inception of the study, fieldwork, data analysis, project management. All authors contributed to manuscript drafting and approved the final  
160 submission, with **JRS** guarantor of the paper.

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### **Competing interests**

165 The authors declare that there are no competing interests.

### **Ethical approval**

Liverpool School of Tropical Medicine Research Ethics Committee, UK (17–018) and National Health Sciences Research Committee, Malawi (1805). Written informed consent was obtained from the child’s guardian before study enrolment, with later on site treatment with praziquantel.

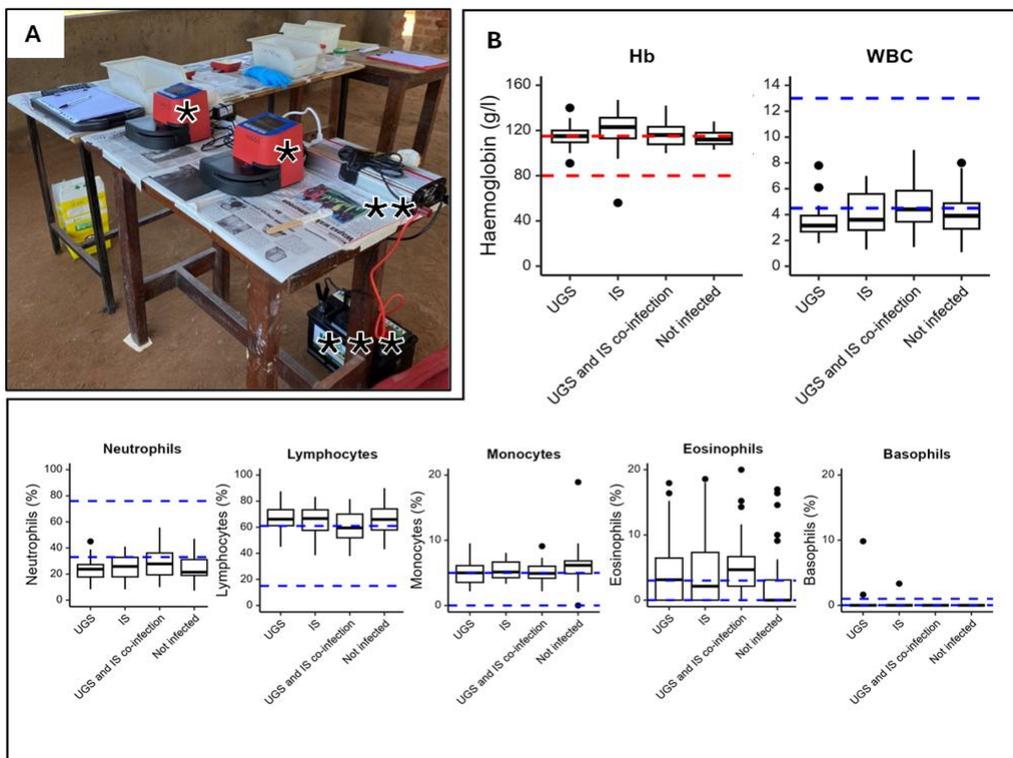
### 170 **Data availability**

All data reported here are available upon reasonable request to JRS.

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**Figure 1.** Use of POC dWBC in Malawi with graphical box-and-whisker plots of seven haematological parameters obtained. **A)** Typical field setup of the phlebotomy work station with a school with two HemoCue® WBC DIFF (\*) analysers in situ, the AC/DC inverter (\*\*), and the 12V enhanced flooded battery (\*\*\*). **B)** Hb (g/l) and WBC ( $\times 10^9/l$ ) results for each infection condition, with white cell differential shown as percentage of total white cells. Upper and lower red dotted lines on Hb plot denote widely accepted anaemia and severe anaemia cut-offs. Upper and lower blue dotted lines on white cell plots denote upper and lower limits of normal. Normal values (absolute and %) taken from [4]. Hb = haemoglobin, WBC = white blood cell; UGS = urogenital schistosomiasis; IS = Intestinal schistosomiasis. It should be noted that normal dWBC values are defined using American- and European-centric standards as there is, at present, no consensus reference values for African participants. N = 120 (total), n for each infection category = 36 (UGS), 17 (IS), 35 (UGS and IS co-infection) and 32 (negative).



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