

FEVER AND LEUCOCYTOSIS IN CHILDREN IN CLINICAL PRACTICE IN SOUTHEAST NIGERIA: THE ROLES PLAYED BY MALARIA AND BACTERIAL INFECTION.

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SUMMARY

Objective: The study was conducted with a view to determining the veracity of the assumption in clinical practice in the tropics that fever with a neutrophilic leucocytosis is more likely due to bacterial infection than to malaria.

Method: A retrospective analysis of case files of children aged over 3 months who had fever of $>38.5^{\circ}\text{C}$ and leucocytosis with a final empirical therapeutic diagnosis of either malaria or bacterial infection, seen over a 3yr period in a paediatric private practice was done. A total of 186 patients comprising 118 treated for malaria and 68 treated for bacterial infection fitted the criteria and were analyzed.

Results: In all the patients with leucocytosis of 11 to $14 \times 10^9/\text{l}$, malaria accounted for 81.7% and a further 60.5% of those with leucocytosis greater than 14 to $17 \times 10^9/\text{l}$. Bacterial infection accounted for 52% and 53.2% of patients with leucocytosis of >17 to $20 \times 10^9/\text{l}$ and $>20 \times 10^9/\text{l}$ respectively ($X^2=18.64$, $X^2_{3,0.05}=7.81$. $P<0.05$).

Considering the neutrophils, malaria accounted for 77.9% of patients with neutrophils of $\leq 75\%$, while bacterial infection accounted for 87.8% of patients with $>75\%$. Again, 95.8% of all malaria patients had neutrophils of $\leq 75\%$ while 52.9% of those with bacterial infection had $>75\%$ neutrophil percent.

Further analysis showed that 78.9% of malaria patients with Hb ≤ 5 gm/100ml had leucocytosis of $>17 \times 10^9/\text{l}$ ($X^2=35.4$, $X^2_{3,0.05}=7.81$ $P<0.05$).

Conclusion: Non-neutrophilic leucocytosis of moderate degree in febrile children in this environment is seen to be due mainly to malaria and this is more so if such patients are anaemic. Care should therefore be taken when interpreting such results.

Key Words: Fever, Febrile illness, children, tropics, leucocytosis

INTRODUCTION

The white blood corpuscle (WBC) count, also referred to as the leucocyte count, is a useful investigative tool in patient management. The total and differential WBC counts are diagnostic in some disease conditions¹. The total count has a normal range of 4 to $11 \times 10^9/\text{l}$ in Caucasians^{1,2} and 3 to $11 \times 10^9/\text{l}$ in blacks.³ WBC counts above these upper limits are considered as leucocytosis¹ and in clinical practice, this is usually secondary to bacterial infection.⁴

Fever is said to be present when the normal body temperature of about 37.2°C is exceeded.⁵

Fever and leucocytosis in bacterial infection results from the presence of bacteria which leads to an increase in phagocytic leucocyte count¹ and the pyrogens released by these bacteria will give rise to a raised body temperature from the resetting of the hypothalamic temperature set point.^{4,5}

In clinical practice in the tropics, especially the sub-Saharan region, febrile episodes tend to commonly result from either malaria or bacterial infection.⁶ Initial differentiation between bacterial infection and malaria is often done with a WBC (total and differential) count; a neutrophilic

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Accepted for publication 8th January 2002

leucocytosis is often considered bacterial infection pending the outcome of blood culture results.

This retrospective study was to ascertain to what extent this view holds true in this environment.

MATERIALS AND METHODS

A retrospective review of folders of febrile patents with final diagnosis of malaria or bacterial infection seen between Jan 1997 and Dec 1999 (inclusive) in a private Children Specialist hospital located in South-east Nigeria was done.

The patients whose folders were used were more than 3 months old and they also had laboratory evidence of leucocytosis.

These patients selected also had either been treated for malaria or bacterial infection with good response.

All the patients who had mixed infections, sickle cell disease and or glucose-6-phosphate dehydrogenase deficiency were not included.

The total WBC count (10⁹/l), neutrophils %, and Hb gm/100ml of each patient that met the criteria were documented.

The findings were subjected to X² analysis and the critical values determined.

RESULTS

A total of 5400 cases were seen in the hospital within the period in review. Out of these, 3115 were cases with febrile illness and of these, a total of 1131 had their Full Blood Count (FBC) done. These results showed leucocytosis in 386 and of these, 186 fitted the criteria and were analyzed. In all, 118 (63.4%) were found to be patients that had malaria while the rest 68 (36.6%) had bacterial infection.

Table 1 shows the leucocytosis levels for the patients with malaria and bacterial infection and Table 2 shows the Hb gm/100ml levels in these patients.

Table 2
Number of patients with Malaria and Bacterial infection at different Hb gm/100ml ranges.

	<=5	5.17 7.1-9	>9	Total	
Malaria	19 *(16.1%) **(100%)	25 *(21.2%) **(89.3%)	49 *(41.5%) **(59.8%)	25 *(21.2%) **(43.9%)	118 (100%)
Bacterial infection	0 *(0%) **(0%)	3 *(4.4%) **(10.7%)	33 *(48.5%) **(40.2%)	32 *(47.1%) **(56.1%)	68 (100%)
Total	19	28	82	57	186

X² = 28.79, X²_{3,0.05} = 7.81.

P < 0.05

Key

- * row percentages
- ** column percentages

For all the patients with malaria, 113 (95.8%) of them had neutrophil % of <=75% while the remaining [5 (4.2%)] had neutrophil % of >75%. Thirty-six or 52.9% of the patients with bacterial infection had neutrophil % of >75% while the others, [32 (47.1%)] had neutrophil % of <=75%.

For all the 145 patients with neutrophil % of <=75%, malaria accounted for 113 (77.9%) of them while bacterial infection accounted for the rest [32 (22.9%)]. On the other hand, while malaria accounted for 5 (12.2%) of all the 41 patients with neutrophil % of >75%, 36 (87.8%) of them were accounted for by bacterial infection. (X² = 59.47, X²_{1,0.05} = 3.84 P < 0.05)

Table 3
Number of patients with Malaria at different total WBC count levels matched against Hb gm/100ml levels.

	<=5	5.7	7.1-9	>9	Total
<=17x10 ⁹ /l	4 *(4.8%) **(21.1%)	15 *(7.9%) **(60%)	42 *(50%) **(87.5%)	25 *(27.4%) **(88.5%)	84 (100%)
>17x10 ⁹ /l	15 *(44.1%) **(78.9%)	10 *(29.4%) **(40%)	6 *(17.6%) **(12.5%)	3 *(8.8%) **(11.5%)	34 (100%)
Total	19	25	48	26	118

12 = 35.4, X²_{3,0.05} = 7.81

P < 0.05

Key;

- * row percentages
- ** column percentages

Table 1
Number of patients with Malaria and Bacterial infection at different total WBC

	<14	>14-17	>17-20	>20	Total
Malaria	58 *(49.2%) **(81.7%)	26 *(10.2%) **(60.5%)	12 *(10.2%) **(48%)	22 *(18.6%) **(46.8%)	118 (100%)
Bacterial infection	13 *(19.1%) **(18.3%)	17 *(25%) **(39.5%)	13 *(19.1%) **(52%)	25 *(36.8%) **(53.2%)	68 (100%)
Total	71	43	25	47	186

X² = 18.64, X²_{3,0.05} = 7.81

P < 0.05

Key

- * row percentages
- ** column percentages

Table 3 shows the relationship between Hb gm/100ml levels and leucocytosis values in the patients with malaria while Table 4 shows this relationship for the patients with bacterial infection.

Table 4
Number of patients with Bacterial infection at different total WBC count levels matched against Hb gm/100ml levels.

	<=9	>9	Total
11-14x10 ⁹ /l	7 *(58.8%) **(18.9%)	6 *(46.2%) **(19.4%)	13 (100%)
>14-17x10 ⁹ /l	8 *(47.1%) **(21.6%)	9 *(52.9%) **(29%)	17 (100%)
>17-20x10 ⁹ /l	8 *(61.5%) **(21.6%)	5 *(38.5%) **(16.1%)	13 (100%)
>20x10 ⁹ /l	14 *(56%) **(37.8%)	11 *(44%) **(35.5%)	25 (100%)
Total	37	31	68

$X^2=0.63, X^2_{3,0.05}=7.81$
 $P>0.05$

Key;

- * row percentages
- ** column percentages

DISCUSSION

Often times, leucocytosis in association with fever is considered to be due to bacterial infection. This retrospective study however shows that leucocytosis of <17x10⁹/l maybe due to malaria infestation (table I), more so if the neutrophil count is normal, malaria accounting for 81.7% of all patients with WBC of <=14x10⁹/l and a further 60.5% of patients with WBC of 14-17x10⁹/l. Most of these patients with malaria (95.8%) had neutrophil % of <=75%. ($X^2=18.6, X^2_{3,0.05}=7.81 P<0.05$). Malaria is a protozoan parasitic infestation that is often marked with monocytosis.^{1,2} This apparently altered response in these children, a subject for probable further research, may however be a consequence of the ability of marrow cells to respond with production of polymorphs and monocytes when stimulated as observed in animal experiment.⁴

Bouts of malaria fever destroy a large number of red cells,^{2,7} and this occurrence of anaemia in association with malaria is observed in this study (Table II). In these patients, malaria accounted for 100% of patients with Hb of

<=5gm/100ml and a further 89.3% of patients with Hb of 5.1 – 7 gm/100ml. On the other hand, bacterial infection accounted for 40.2% and 56.1% of all patients with Hb of 7.1 – 9gm/100ml and >9gm/100ml respectively. This invariably means that bacterial infection as found in this group of patients does not cause significant anaemia.

Furthermore, relating the leucocytosis in malaria cases to their Hb values (table III), it is observed that at Hb of <=5gm/100ml, 78.9% of the patients had leucocytosis of >17x10⁹ /l. On the other hand, at Hb level >5gm/100ml, leucocytosis in malaria tended to be <=17x10⁹/l. Though low red and white cell count can occur in malaria,^{2,8} this review however has shown that leucocytosis with normal neutrophil % can be seen in malaria, especially if such patients are pale. This association of anaemia and leucocytosis in malaria may be as a consequence of the same mechanism or as a result of malaria giving rise to acute red cell lysis, a factor known to cause leucocytosis,^{1,4} hence the association. Bacterial infection in these patients did not show this trend and its X² analysis was statistically insignificant.

These findings may further give credence to the fact that malaria is a great mimic. On the other hand, the roles played by the age of these cases (non-immuned or semi-immuned), the tropical environment, the parasitic load and also the possibility of prior drug consumption were not evaluated.

Dagan et al¹⁰ had studied 233 infants that were less than 3 mths old admitted for sepsis in their environment. Of the 67% of these infants in whom the causative organisms in their illness were identified, viruses accounted for 58% of the organisms cultured while sepsis accounted for only 8%. Their study was in temperate region where viruses seem to predominate. In this environment where malaria predominates, this present retrospective study has shown that malaria can greatly mimic the findings often seen in bacterial infections.

CONCLUSION

This study has shown that leucocytosis especially with normal neutrophil count in febrile children most probably results from malaria. This becomes more certain if such children are also anaemic. It is therefore necessary for practicing clinicians to be careful how much premium is placed on WBC counts while evaluating their

patients for bacterial infection in this environment and possibly other malaria zones.

ACKNOWLEDGEMENT

We wish to express our profound gratitude to the management of Prime Concept Consultants, Children Specialist Hospital where the data were collected.

Our appreciation also goes to Prof Bede Ibeh of the Department of Paediatrics UNTH Enugu who made useful corrections to the manuscript.

REFERENCES

1. Baker F.J, Silvertown R.E. Introduction to Haematology: In Baker F.J, Silvertown R.E. (eds.): Introduction to Medical Laboratory Technology. Sixth edition. Butterworths. London. 1985. 306.
2. Dagg J., Lee F. D: Blood and Bone marrow: In Anderson R. (ed). Muir's Textbook of Pathology, Tenth edition. English Language Book Society and Edward Arnold (Publishers) Ltd. London. 1976. 450.
3. Ukaejiofo E.O., Isaacs-Soyede W.A., Adigun E.S., and Ipadeola A. Normal haematological values in adult Nigerians. *Nig. Med. J* 1979; 9(1) 117-119.
4. Anderson J. R: Infections: Host-Parasite relationships: In Anderson J. R (ed). Muir's Textbook of Pathology. Tenth edition. English Language Book Society and Edward Arnold (Publishers) Ltd. London 1976. 144.
5. F. R. Henretig F.R. Fever: In (J.Fleisher, S. Ludwig (eds.): Textbook of pediatric emergency medicine. Third edition. Lippincoll Williams and Wilkins. U.S.A. 1993. 163.
6. W. H. O. Fact Sheet No94; 1998.
7. Hutchisons J. H. (ed). Practical paediatric problems. Fifth edition. Pitman Press. London 1980. 647
8. John T.J., Heyneman D. Infections: Parasitic: In Kempe H., Silver H. K., O'Brien D (eds.): Current Paediatric Diagnosis and Treatment. Fourth edition. Lange Medical Publications. California. 1976. 760
9. Dagan R., Hall C.B., Powell K.R. et al: Epidemiology and laboratory diagnosis of infections in infants hospitalised for suspected sepsis. *J. Pediatr* 115 (3) 1989. 351- 6.