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Prediction of Dermatophyte Culture by Clinical Features: Saving Time and Cost in Resource-Poor Settings

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Abstract
Background: *Tinea capitis* is common among children worldwide. Confirmation of diagnosis for early commencement of therapy and control has continued to be a major challenge in resource-poor settings. **Patients and Methods:** This cross-sectional study recruited 185 children in the rural community of Osogbo, Nigeria. Two thirds of the study population were children aged 5 to 8 years. Clinical history was documented and scalp scrapping of scales and hairs was obtained for microscopy and culture. Two sided fisher exact test was employed in the bivariate analysis. **Results:** The mean ± SD age for the culture positive and the negative children were 7.2 ± 2.2 years and 7.8 ± 2.7 years respectively. Dermatophyte culture positivity was found in 123 (66.5%) of the children. For the culture-positive children, the positive predictive values were high at 95%, 91%, 88%, and 87% and negative predictive values were low at 16%, 24%, 18% and 0% respectively for adenopathy, alopecia, pruritus, and scalp scaling as single symptom and sign respectively. For various combinations of any two symptoms, positive predictive values ranged from 73-82%, for three symptoms 81% and for four symptoms 77%. The

combinations also demonstrated higher negative predictive values 67 – 86% for two, 64% for three and 78% for four symptoms, the absence of which diagnosis could be held in doubt. Similarly, positive likelihood ratios were 2.7, 1.5,1.1, and 1.0 for adenopathy, alopecia, pruritus, and scalp scaling respectively. The positive likelihood ratios ranges from 1.6 – 2.8 for various combinations of two cardinal symptoms; highest for adenopathy and alopecia, and 2.0 for three symptoms and 1.8 for all the four symptoms. **Conclusions**: Among pre adolescent children, culture positivity is well predicted when adenopathy and alopecia are present or in combination with scalp scaling. Consequently, control of infection may be further enhanced with omission of culture and early commencement of treatment.

Key word; *Tinea capitis*; dermatophyte culture; symptoms and signs.

Introduction
Tinea capitis (TC) is an infectious dermatological disease of a major public health importance in the sub-tropics. The disease remains an index of the poor socio-economic situ-

ation that is still ravaging the region. The prevalence rates of TC ranges broadly from 4% to 30% among school children in Western and Southern Africa (1,2). Despite being a common condition in the tropics, misdiagnosis of TC still occurs too often in clinical practice (3). Non-availability of equipment and trained personnel also remain the bane of management in many rural and suburban settings in Nigeria. Even in places where resources are available, parents and children are faced with the challenge of unaffordable high cost of investigations and long waiting time in getting the culture result. In some parts, children are even kept out of school to prevent infecting other children with a resultant loss of school hours. *Tinea capitis* therefore poses a major challenge for the rural health workers, parents of affected children and the children themselves. There is a need therefore for the availability of an efficient, affordable, and reliable framework, upon which diagnosis and treatment can be reliably based within the economic limitations of the developing nations (4,5). Similar studies have been conducted elsewhere but none exist in a large country like Nigeria where the pain is felt most. The aim of this study was to evaluate a composite framework based on symptoms and signs upon which diagnosis and treatment could be based in order to control the spread of the disease among children.

Patients and Methods
Settings and Protocol
A cross-section design was used. Ethical approval was granted by the ethical committee of Ladoke Akintola University Teaching Hospital, Osogbo, Osun state. The subjects of this study were children recruited randomly from the Ilie community of Olorunda local government area of Osogbo, Osun State, Nigeria between August 2010 and January 2011. The reasons for and benefits of the study were explained in clear terms to the participating parents and their children. Informed consent was obtained from parents whose children were included. Evening house to house survey of symptom (s) and sign (s) suggestive of TC was conducted in the village, when parents and children have retired to their homes after the day's work.

Study Population
One hundred and eighty five children were randomly recruited through multistage sampling method, comprising of multiple random samplings from homes in different communities, compounds and houses. Scalp symptoms or signs such as pruritus, scaling, hair loss (patchy or diffuse), and presence of visible and palpable posterior cervical and or occipital adenopathy as reported by the children or no-

ticed by their parents were documented. Following this, the children had all areas of their scalp thoroughly examined for clinical signs of TC and adenopathy. Cases of atopic dermatitis, pustular folliculitis, suspected pustular type of TC and or kerion were excluded. Other exclusion criteria included presence of significant lymphadenopathy outside occipital and cervical area, inflammatory dermatosis, previous or on-going treatment with any form of antifungal agents topical or orals. Sufficient scrapped samples were obtained from 185 children.

Laboratory assessments
The area of the head affected was cleaned with alcohol, hairs and scales were collected into dry, clean envelope for mycological examination using the technique described by Fathi et al. (3). The hair scrapping was transported from the field in a dry and clean envelope. Direct microscopy using 10% potassium hydroxide was done to examine for fungal elements. The scrapings and the pieces of hair were also plated out immediately as soon as the investigator arrived from the field on daily basis separately on culture media. The dermatophyte potatoes specific culture agar was used. Two culture plates were used for each isolates, the culture plates was incubated both at the room temperature (25°C) and at 37°C for 4 weeks and then macro and micro morphological studies of cultured colonies were done for the presence of dermatophytes. *Tinea capitis* was diagnosed clinically at the presence of cardinal symptom(s) and or sign (s). Diagnosis was doubted when symptom (s) and or sign (s) were doubtful or non-specific. We defined true positivity as the clinical diagnosis of TC with cultured positivity. True Negativity were those situation when diagnosis was doubtful and with negative culture result for dermatophyte. False positivity was defined as the presence of symptoms and signs with negative culture. Meanwhile, we defined false negativity as those cases when clinical diagnosis was doubtful and but dermatophyte culture was positive. All the culture positive children received incentive oral micronized Griseofulvin at a dose of 15mg/kg body weight for 8 weeks. All samples for culture were obtained before the incentive treatment.

Statistical Analysis
Data were entered into a statistical software program (SPSS Chicago Inc., IL, U.S.A., V 16.0). The 185 sample size was calculated to measure a TC of 50% with an absolute precision of 1% and a confidence interval of 95% and to have more than 95% power to detect significant association between symptoms and signs and positive culture consid-

ering similar previous studies (4, 5). The two sided fisher exact test was employed in the bivariate statistical analysis. Demographic characteristics were summarized using descriptive methods as appropriate. The presence and absence of individual sign and symptoms were documented and whether culture were positive or negative were noted with corresponding symptoms and signs. The positive and negative likelihood ratios and positive and negative predictive values were calculated for each individual sign and symptom and for their combinations. The likelihood ratio (LR) values above 1.0 were recorded to the nearest decimal place; while LRs below 1 were recorded to the nearest 0.1. Using the standardized table of likelihood ratio and bedside estimates by McGeep (6), the approximate change in probabilities were estimated. Positive Likelihood ratio (PLR) describes probability shift of disease when a symptom or sign is present, while Negative Likelihood ratio (NLR) describes the probability shift of disease shifts when such symptom or sign is absent (6). Positive predictive value (PPV) is the probability a patient will have a condition given a positive test. Negative predictive value (NPV) is the probability a patient will not have the disease given a negative test (7). P was taken to be significant at < 0.05

Results
Clinical Characteristics
The mean±SD ages were 7.2±2.2 years and 7.8±2.7 years for culture-positive and culture-negative children respectively. Male gender was prevalent for both cultures positive and negative children, with male:female ratio of 2.3:1 and 2:1 respectively.

Direct Microscopy and Culture
Direct microcopy identified fungal elements in 88% of the samples and 66.5% of the children had positive dermato-

phyte culture. 9.1% of the scrapped samples had a negative culture after incubation for 28 days. Culture positivity rate was highest for children aged 5-8 years at 53.0% while those aged 9-12 years and 13-16 years had lower positivity rates of 8.7% and 4.9% respectively (Table 1). Scaling was the commonest symptom found among 96.8% of the participants, while scalp pruritus, alopecia and adenopathy were found in 87.0%, 75.1% and 25.4% of the participants respectively (Table 2). The rate of culture positivity from single sign or symptom was the highest with presence of adenopathy (76.6%) and alopecia (66.2%). On the other hand, culture negativity was least with same symptoms/signs at 4.3% and 6.5% respectively. The rate of culture positivity for scalp scaling was 65.8% and for pruritus was 65.4%. Although the duos were the most common presenting symptoms and or signs respectively, they both had higher rate of culture negativity and false positivity, as shown in Table 2. Combinations of symptoms and or signs did not imply higher rate of culture positivity for most combinations (Table 2). However, the rate of culture positivity was highest with combination of alopecia and adenopathy, alopecia with scaling and much lower when multiple of three and four symptoms/signs were combined (Table 2). The rate of culture negativity and false positivity was least with the presence of alopecia with adenopathy and highest with alopecia and scalp scaling combination (Table 2).

Clinical Prediction from Culture Results
We estimated the PLR, NLR, PPV, and NPV of individual and combinations of sign and symptom of *TC* from culture results were as documented in Table 3. The single presence of individual symptom and sign gave a PLR ranging from 1 – 2.7 and gave NLR which ranged from 0 – 0.7 which insignificantly decreased likelihood of diagnosis by 0 to

Table 1. The distribution of children's age in relation to symptom / sign, Potassium hydroxide and culture					
Age groups (years)	Number with symptom/sign	KOH Examination N (%)		Culture N (%)	
	N (%)	Positive	Negative	Positive	Negative
5 – 8	139 (75.13)	126 (68.10)	13(7.03)	98(53.0)	8(4.32)
9 – 12	35 (18.92)	28(16.14)	7 (3.78)	16(8.65)	7(3.78)
13 – 16	11 (5.95)	9(4.86)	2(1.08)	9(4.86)	2(1.08)
Total	185 (100)	163(88.11)	22(11.89)	123(66.5)	17(9.18)
N = number, % = percentage, KOH = Potassium hydroxide					

Table 2. Individual symptom/ sign of Tinea capitis their combinations in relation to culture				
	Culture-positive (%)	Culture-negative (%)	False positive (%)	False negative (%)
Any Sign or Symptom				
Adenopathy (47)	36 (76.6)	2 (4.3)	8 (17.0)	1 (2.1)
Alopecia (139)	92 (66.2)	9 (6.47)	35 (25.2)	3 (2.2)
Pruritus (161)	106 (65.8)	15 (9.3)	35 (21.7)	5 (3.1)
Scaling (179)	117 (65.4)	18 (10.1)	40 (22.4)	4 (2.2)
Combination of Signs and Symptoms				
Alopecia/adenopathy (33)	22 (66.7)	4 (12.1)	5(15.2)	2(6.1)
Scaling/Alopecia (136)	85(62.5)	18(13.2)	30(20.4)	3(2.0)
Scaling/Adenopathy (47)	27(57.4)	8(17.0)	10(21.3)	2(4.3)
Scaling/Adenopathy/Alopecia (37)	21(56.8)	7(18.9)	5(13.5)	4(10.8)
Scaling/Alopecia/Pruritus / Adenopathy (44)	27(61.4)	7(15.9)	8(18.2)	2(4.5)
N= Number; %= Percentage				

-5%. In this profile, adenopathy and alopecia gave PLR of 2.7 and 1.5 respectively and increased probability of culture positivity to 63.5% (43.5± 20%) and 58.5% (43.5% ± 15%) respectively. The profile of PPV with culture results for single symptoms or signs ranges from 87% - 95%. Adenopathy and alopecia were responsible for the highest PPV of 95% and 91% respectively. However, the profiles of NPV for single symptoms/signs were low and ranges from 0% – 24% as documented in Table 3. The present study shows that, the combinations of symptoms and signs gave a similar increase in PLR as the single symptom and sign. The PLR ranges from 1.6 – 2.8 and NLR which ranges 0.1 – 0.3 with various combinations. In the same vein, the profile of PPV ranges from 73% - 82% for various combinations. The PPV was highest with adenopathy and alopecia (82%), followed by adenopathy,alopecia and scalp scaling (81%) and least with scaling and adenopathy (73%). However, the combinations of these symptoms and signs gave higher profile of NPV that ranges from 64% to 86%. The different combinations of two, three and four signs/symptoms gave higher NPV for culture positivity than single symptom or sign as shown in Table 3.

Discussion

Dermatophytosis is a disease of the major public health problem worldwide (1, 8). Presently, it is widely distributed and is affecting more than 20-25% of the world's population (9). Of these, children of pre pubertal age group between 4 and 14 years are disproportionally affected because of frequent body contact (10). The difficulty associated with diagnosis of TC can be attributed to its nonspecific clinical presentation of the disease (4). In certain circumstance when ringworm is been suspected, confirmation may be problematic because some practitioners have no means of confirming it in good time (4), and this is worse in rural sub Saharan Africa settings. The diagnosis of tinea infection of the scalp can usually be suspected clinically but microbiology confirmatory diagnostic test is necessary (11).

Previous studies reported the sensitivity of fungal culture in identifying dermatophytes as varying widely from 25% to 80% with approximately 30% false-negative results with culture and KOH studies (12-15). The microscopic examination of scrapping in our study identified fungal element in 88.1% which is half way between the previous reports of 95.5% by Ajao et al. (17) and 79.5% by Soyinka et al. (18).

Table 3. The likelihood and predictive characteristics of symptom (s) and sign(s) of Tinea capitis in relation to dermatophyte culture.

Sign/symptom (N)	PLR	NLR	NPV	PPV
Adenopathy (47)	2.7	0.7	16%	95%
Alopecia (139)	1.5	0.5	24%	91%
Pruritus (161)	1.1	0.7	18%	88%
Scaling (179)	1.0	0.03	0%	87%
Combination of Signs and Symptoms (N)				
Alopecia/adenopathy (33)	2.8	0.2	67%	82%
Scaling/Alopecia (136)	1.6	0.1	86%	74%
Scaling/Adenopathy (47)	1.7	0.2	80%	73%
Scaling/Adenopathy/Alopecia (37)	2.0	0.3	64%	81%
Scaling/Alopecia/Pruritus/ Adenopathy (44)	1.8	0.2	78%	77%

N = Number, PPV = positive predictive value; and NPV = negative predictive value, PLR = positive likelihood ratio; NLR = negative likelihood ratio

Similarly, culture negative rate was close to that obtained by previous workers (15,17). Culture negativity can be reduced by biochemical methods as employed by Emeka (14) in his study. The high growth rate of non-dermatophyte fungi 21.6% in this study might not be unconnected with the high humidity and the poor level of hygiene in the village environment. Other sophisticated means of improving dermatophyte yield are not widely available due to financial restrictions (13,14).

In this study we examined the possibility of using specific clinical signs and or symptoms to design a frame work upon that will predict culture positivity within a limited resource setting, upon which diagnosis can be based, for early treatment to save time, cost reduction and prompt reduction of infection in circulation. The age of children affected in our study is similar to the findings of other workers world-wide (16) and culture positivity decreases as the age of recruited children increases. Scalp scaling (96.8%) was the commonest complaint and examination finding among children with TC. The rate of scalp scaling in the present study falls within 80 – 100% previously documented in other studies (16,19). The prevalence of scalp pruritus (87.0%), alopecia

(75.1%), and adenopathy (25.4%) were also similar to findings of Hubbard (4) who looked at 100 children in a hospital based study. Similarly, previous studies have recognized patchy hair loss as the cardinal feature (4, 5) while itching was noted as a variable feature of TC (20). The frequency of adenopathy (25.4%) as a symptom or sign falls below previously quoted range of 42% to 72% by Ravits et al, (21) and 90% reported by Hubbard (4). This might not be unconnected with the fact that, only significant adenopathy in the occipital and posterior cervical chain was taken into consideration in our study, while Hubbard (4) and other workers (21) included any degree of adenopathy in their series.

The PPV of single symptoms or signs found in our study were comparable to the findings of other studies (4,5). For adenopathy, we found PPV of 95% while others found 94 % (4), and 84% (5) respectively. Positive predictive value was 91% for alopecia in the present study, other workers found 84% (4), and 80% (5). Pruritus positively predicts culture by 88%; other workers documented a PPV of 75% (4) and 77% (5). We found PPV of 87% for scalp scaling, Hubbard (4) and Kelly et al. (5) found 71%, and 79% re-

spectively in their studies. While culture positivity for adenopathy was 100% and its presence with patchy hair loss predicted culture positivity the most in a foreign study (4), however in the present study, culture positivity for adenopathy was 76.6% (36/47), with high PPV of 95% and lower NPV of 16%. The presence of adenopathy in combination with other symptoms such as alopecia and scaling gave better profile of predictive power for dermatophyte culture. There was no such association between positive culture and the number of symptoms in this study (P > 0.05) in difference to Hubbard's study (4) and in agreement with Kelly et al. study, (5) such that the profile of PPV given by single symptoms and signs were close to profile of different pairs, triad and all the four symptoms. The single symptom/sign though demonstrated higher PPV also had lower NPV which decreased the probability of culture positivity when such symptoms or signs are absent than the combinations of symptoms and signs.

The combinations of multiple symptoms and signs gave slightly higher PLR which increased probability of positive culture than individual single symptom and sign. These combinations also gave much lower profiles of NLR which implied that, in the absence such combination, the diagnosis of TC should be held in doubt in this setting. This observation is similar to that of Kelly et al. (5) but different from the conclusion drawn from other study (4) that signified higher likelihood of culture positivity among children with adenopathy. In this study, occipital and or posterior cervical adenopathy and alopecia seem to be the most important signs/symptoms. The presence of adenopathy significantly reduces the rate of false positivity to 13.5% when present with scaling and alopecia, and to 15.2% when present with alopecia alone. The possibility of over treatment, which could be a concern with this frame work is reduced to a bare minimum. The two symptoms are important because the dermatophytes as keratophilic organism invade the scalp hair and the lymphatic channel of the scalp drain into the regional lymph nodes (occipital and posterior cervical), and this probably marks the presence of the dermatophyte infection on the scalp the most. Scalp scaling singly was the least important cardinal symptom in the diagnosis of TC in this study. Scaling becomes important only when adenopathy and alopecia are present. We therefore suggest that, among pre adolescent children and others in similar settings, clinical diagnosis of TC can be reasonably suggested using combinations of the important symptoms or signs like adenopathy, alopecia, and or scaling in agreement with previous suggestions (5,22). Working with this

frame work in rural setting with shortage of dermatologist and other health care giver could help in combating the increasing spread of the disease. Omitting confirmatory culture could lead to gaining of up to two to four week of waiting time and reduction of period of effective and infective bodily contact in among children in public places. In addition, we could save up to approximately 50 dollars per child in places where prevalence is up to 25% (9) among children. Griseofulvin remains important in the treatment of TC. It is less expensive, and has good safety profile and is available as oral suspension which allows for accuracy of dosing in children (23). If griseofulvin is taken daily over six to eight weeks the chance of resistance is much reduced. Inadvertent use of Griseofulvin could be another concern with this type of frame work and that could be prevented in such setting by strict adherence to component symptoms that predict culture before diagnosis for commencement of oral therapy. We also suggest that government at local level could make drug available at affordable price to curb the menace of the spread of TC.

In conclusion, the presence of cardinal symptoms or signs of TC such as adenopathy in combination with other symptoms like alopecia or scaling predict dermatophyte culture positivity among pre adolescent children. Children with TC infection in a resource and personnel scarce primary care environment can be empirically commenced on antifungal treatment without having to wait for culture result.

References
1. Ekanem LS, Gugnani HC. Etiology of dermatophytoses amongst school children in Cross River State, Nigeria. Mykosen 1987;30:493-8.
2. Simpania MF. A contribution to the study of tinea capitis in Lusaka, Zambia. E Afr med J 1989;66:269-75.
3. Fathi HI and Al-Samarai AGM. Prevalence of tinea capitis among schoolchildren in Iraq. Eastern Mediterranean Health Journal. 2000;6(1):128-37.
4. Hubbard, TW. The predictive value of symptoms in diagnosing childhood Tinea Capitis. Arch Pediatr Adolesc Med. 1999;153:1150-3.
5. Lorch Dauk KC, Comrov E, Blumer JL, O'Riordan MA, Furman LM. Tinea Capitis: Predictive value of symptoms and time to cure with Griseofulvin treatment. Clin Pediatr. 2010;49(3):280-6.
6. McGeep S. Simplifying likelihood ratios. J Gen Intern Med. 2002;17(8):647–50.
7. Spitalnic S. Test properties, Sensitivity, specificity, and

predictive values. Hospital Physician 2004;40(9):27-31.

8. Pariser DM. Superficial fungal infections. A practical guide for primary care physicians. Postgrad Med 1990;87:205-14.

9. Aghamirian MR, Ghiasian SA. Dermatophytoses in outpatients attending the dermatology center of Avicenna hospital in Qazvin. Mycoses. 2008;51(2):155-60.

10. Bassiri-Jahromi S, Khaksar AA. Epidemiological survey of dermatophtosis in Tehran, Iran, from 2000-2005. Indian J Dermatol. 2009;75(2):142-7.

11. Jordan HF. The diagnosis and management of Tinea capitis. SA Pharmaceutical J. 2006;8-11.

12. Suarez SM, Silvers DM, Scher RK, Pearlstein HH, Auerbach R. Histopathologic evaluation of nail clippings for diagnosing onychomycosis. Arch Dermatol. 1991;127:1517-9.

13. Honig PJ, Sullivan K, McGowan KL. The rapid diagnosis of tinea capitis using calcofluor white. Pediatr Emerg Care. 1996;12:333-5.

14. Nweze EI. Dermatophytosis among children of Fulani/Hausa herdsmen living in southeastern Nigeria: Rev Iberoam Micol. 2010;27(4):191-4.

15. Yazdanfar A. Tinea capitis in primary school children in Hamedan (West of Iran). International Journal of Medicine and Medical Sciences. 2010;2(2):29-33.

16. Smith ML. Tinea capitis. Pediatr Ann. 1996;25:101-5.

17. Ajao AO, Akintunde CA. Studies on the prevalence of *Tinea capitis* in Ile-Ife Mycopathologia. 2005;89:43-8.

18. Soyinka F. Epidemiologic study of dermatophyte infections in Nigeria (Clinical Survey and Laboratory Investigations). Mycopathologia. 1978;63(2):99-103.

19. Babel DE, Baughman SA. Evaluation of the adult carrier state in juvenile tinea capitis caused by Trichophyton tonsurans. J Am Acad Dermatol. 1989;21:1209-12.

20. Gugnani HC, Njoku-Obi ANU. Tinea capitis in school children in East Nigeria. Mykosen. 1986;29:132- 4.

21. Ravits MS, Himmelstein R. Tinea capitis in the New York City area. Arch Dermatol. 1983;119:532-3.

22. Coley MK, Bhanusali DG, Silverberg JI, Alexis AF, Silverberg NB. Scalp hyperkeratosis and alopecia in children of color. J Drugs Dermatol. 2011;10(5):511-16.

23. Tey HL, Tan ASL, Chan YC. Meta-analysis of randomized, controlled trials comparing Griseofulvin and Terbinafine in the treatment of tinea capitis. J Am Acad Dermatol 2011;64:663-70.