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Table of Content

Editorial	Pg No
Approach to Severe Asthma Ramesh Kumar Suthar	1
Original Articles	
Frequency of Depression Among Teenagers with Asthma Zaheer Hussain Memon, Akbar Memon, Madiha Zaki	03
Comparative Analysis of Immunochromatographic Diagnostic Test and Microscopy for the Detection of Plasmodium Species Shahzad Ali Jiskani, Saira Rajput, Umair Ali Soomro, Sikandar Ali Bhand	10
Maternal Thyroid Status and Its Association with Iron Profile Arshad Ali Lakho, Zahida Zia, Sher Ali, Mubashir Raza, Ashraf Ali	15
Study of Relationship Between Hyperuricemia and Dyslipidemia Ramesh Kumar Suthar, Kavita Bai, Mumtaz Ali Memon, Keenjhar Rani	20
Evaluation of Red Blood Cell Indices in Patients with Falciparum Malaria Shahzad Ali Jiskani, Inayatullah Memon, Umair Ali Soomro, Shumail Siddiqui, Mehnaz Shaikh, Huma Abbasi	27
Letter to Editor	32
Short Course with Long Duration of Azithromycin Shahzad Ali Jiskani	

EDITORIAL: APPROACH TO SEVERE ASTHMA

Ramesh Kumar Suthar

Department of Medicine, Indus Medical College, Tando Muhammad Khan

Corresponding Author:

Ramesh Kumar Suthar

MBBS, MD (Medicine)

Assist. Professor, Department of Medicine
Indus Medical College Tando Muhammad
Khan

Corresponding Author Email:

rk22258627@gmail.com

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Approximately 5-10% of asthmatics are barely controlled or clinically and/or functionally uncontrolled despite a high dose of inhaled corticosteroids (ICS) plus another controller agent (e.g., long-acting beta2-agonists, LABA; leukotriene-receptor antagonists, LTRA; long-acting muscarinic agents, LAMA) or maintenance oral corticosteroid therapy. These patients are defined as affected by "severe asthma" according to the most recent recommendations of the European Respiratory Society (ERS) and the American Thoracic Society.⁽¹⁾

The diagnosis of severe asthma is made after having ruled out or having treated clinical conditions that may mimic asthmatic symptoms (e.g., extra-thoracic hyperresponsiveness syndromes, vocal cord dysfunction), comorbidities that may worsen disease control (e.g., allergic or nonallergic rhinitis, chronic rhinosinusitis with or without nasal polyps, bronchiectasis, and gastroesophageal reflux), possible incorrect inhaler techniques, and/or poor treatment adherence. During the past decade, advanced research brought insight into the heterogeneous mechanisms of severe asthma and helped to reveal several potential therapeutic targets.⁽²⁾

Following the introduction of the first available biologic agents in clinical practice, the way of diagnosing and managing the majority of patients with severe asthma dramatically changed from a "one-size-fits-all" approach to precision medicine.⁽³⁾ Presently, we are experiencing a new era in the management of severe asthmatic patients, as subjects are clinically characterized in phenotypes⁽⁴⁾ or in treatable traits⁽⁵⁾ in order to personalize their disease-management.

In this special issue, the latest knowledge and novel findings in severe asthma pathogenesis, pheno/endotyping and management with a particular focus on personalized and precision medicine approaches, have been addressed.

The classification of patients according to their phenotypes and/or endotypes⁽⁴⁾ is strictly dependent on the identification of reliable biomarkers, ideally non-invasive and available for point-of-care.⁽⁶⁾ The article by Mortaz et al. elegantly summarizes a plethora of possible new biomarkers from tissue-derived exosomes. These small membrane-enclosed vesicles contain mRNA and miRNA, lipids, and a vast array of different proteins depending on their cell of origin. Furthermore, exosomes may also be potentially used for developing novel therapeutic strategies. Galeone et al. pointed their attention on how the new field of "omics" sciences (including proteomics, metabolomics, transcriptomics, and genomics) may provide new biomarkers, novel targets for diagnostic tests, and pharmacological treatments.

This complex scenario of new technologies and biomarkers, applied to the process

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of identification of specific severe asthma phenotypes and endotypes, is part of the precision medicine approach to asthma. The direct consequence of a better characterization of patients under the immunological point of view is the possibility to treat them with novel biologic agents, acting directly towards those immunological mechanisms that are involved in every single endotype of severe asthma.⁽⁷⁾ The first available biologic agent for severe asthma was omalizumab, a fully humanized anti-IgE monoclonal antibody. Its clinical efficacy and effectiveness in severe allergic patients have been proved extensively. There are some recent studies also suggesting effectiveness in non-allergic severe asthmatics. Loureiro et al. reviewed the current evidence on both of these possible uses of omalizumab in this present Special Issue. In the past few years, novel therapeutic targets have been addressed by recently approved biologic agents: mainly, anti-IL5 strategies are currently worldwide used for severe eosinophilic asthma.⁽⁸⁾ Bagnasco et al. overviewed the possible molecular targets and related biologic drugs, blocking the IL5-mediated eosinophilic inflammation in severe asthma.

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FREQUENCY OF DEPRESSION AMONG TEENAGERS WITH ASTHMA

¹Zaheer Hussain Memon, ²Akbar Memon, ¹Madiha Zaki, ¹Ramesh Kumar Suthar

¹Department of Medicine, Indus Medical College, Tando Mohammad Khan

²Department of Medicine, Isra University Hospital, Hyderabad

Corresponding Author:

Zaheer Hussain Memon

MD (Medicine)

Assistant Professor, Department of Medicine,
Indus Medical College Hospital, Tando
Mohammad Khan

Co-Authors:

Akbar Memon

FCPS (Medicine)

Associate Professor, Department of Medicine,
Isra University Hyderabad

Madiha Zaki

MRCP (Gastroenterology),

Consultant Gastroenterologist

Indus Medical College Hospital, Tando
Muhammad Khan

Ramesh Kumar Suthar

MBBS, MD (Medicine)

Assist. Professor, Department of Medicine
Indus Medical College Tando Muhammad Khan

Corresponding Author Email:

drzaheerh@gmail.com

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ABSTRACT

OBJECTIVES: The objective of this study is to determine the frequency of depression among asthmatic teenagers 13 to 19 years of age visiting at outpatient departments of Indus Medical College Hospital Tando Muhammad Khan.

METHODS AND MATERIAL: An observational prospectivestudyconductedattheDepartment of Medicine, Indus Medical College Hospital, Tando Mohammad Khan, Pakistan from December 2017 to July 2018. A total of 262 asthmatic teenagers attending Medicine and Pulmonology clinic, aged 13 to 19 years, who have been diagnosed to have uncontrolled asthma (according to GINA guidelines) for at least one year were included .Demographic profile along with asthma outcomes were compared with age. The p value less than 0.05 was considered as statistically significant.

RESULTS: A total of 262 asthmatic teenager patients were included in this study with mean age + SD 55.49 + 11.67 years. The mean duration + SD (range) of asthma was 5.6 + 1.32 (3 to 8 years). It was found that 30 (11.4%) cases had family history of asthma whereas 45(17.1%) cases had family history of depression. In the present study the total frequency of depression was found to be 37 (14.1%) among the teenagers. In the present study it was observed that gender, duration of asthma, residence, marital status, educational status, socio-

economic status, history of psychiatric illness and employment status were significantly associated with depression(p value <0.05).

CONCLUSION: This study concluded that depression is highly prevalent in patients with asthma among teenagers.

KEYWORDS: Asthma, Teenager, Depression, Frequency

INTRODUCTION

Asthma is the chronic respiratory disease

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that usually affects people of all years of age, characterize by the symptoms of cough, dyspnea, wheezing, and chest tightness. ⁽¹⁾ In United Kingdom around 3.4 millions of children age group 2 to 15 years is suffering from asthma that requires treatment. ⁽²⁾ In Pakistan, a survey done in the area of South Panjab that shows 7% asthma rate which was similar to that found in previous studies involving 12 year old children in Switzerland (5.95%), Chile (8.0%) and in 7-11 year old Asian children in the United Kingdom (6.2%). Higher asthma prevalence was found in children from England (13.1%) and Australia (23.2%). ⁽³⁾

The relationship between psychological morbidity and asthma has been previously recognized. There are many studies suggest that depression related symptoms are more common in asthma patients than compared with the general population. An analytical study done in Japan showed there was a clear association between asthma control and severity, and depression. ⁽⁴⁾ Younger patients with asthma have a high rate of depressive disorders and anxiety, and these psychiatric disorders are associated with the aggravating factors for asthma symptom burden and functional impairment. Approximately 35% of youth with 1 or more are suffering from anxiety and depressive disorders. ⁽⁵⁾

Physicians usually do not emphasis on depressive symptoms in Asthmatic teenagers which lead to increased symptoms and morbidity. Since a majority of asthmatic teenager is treated by primary care provider, screening of depressive disorder could make a management difference. This study aims to find out the burden of depression in asthmatic teenagers.

METHODS AND MATERIAL:

This is a simple, observational, single centre study conducted at Indus medical college Hospital, Tando Mohammad Khan with duration of one year (from December 2017 till July 2018). Data collection was

done prospectively. Study started after getting approval from hospital research and ethical committee. Using WHO Calculator sample size was 262 at 95 % confidence interval. Using non probability consecutive sampling, as the frequency of depression in asthmatic children's of teenage group is 43%, with 6% margin of error.

Teenagers of aged 13 to 19 years visiting Departments of Medicine and Pulmonology, who have been diagnosed to have uncontrolled asthma (according to GINA guidelines) for at least one year were included. Informed consent was taken from all the study participants. Previous history of depression or anti-depressant medication in 3 months was noted. Asthmatic children with other co-morbid disease such as cystic fibrosis, tuberculosis, diabetes, thalassemia, acute exacerbation of asthma requiring hospital admission as assessed by clinician were excluded from this study. Those who lost follow up were also excluded. Participants were interviewed by researcher in a quiet room with privacy after taking an informed verbal and written consent and explaining them about the study. The questionnaire has demographic data such as age, gender, socioeconomic status, and reason for current visits, duration of asthma, education, and family history of asthma and for diagnosis of depression it is incorporated with DSM IV criteria. It takes about 20 minutes to complete. It focuses on symptoms of depression in asthmatics in the past 2 week, to minimize the recall bias.

Data were entered and analyzed in statistical program SPSS version 19.0. simple frequencies and percentages were calculated for qualitative data such as gender, age (in groups), marital status, socio-economic status, place of residence, level of education, family history of asthma and depression and the outcome variable i.e., depression. Mean + SD was calculated for continuous variables like age, weight and duration of asthma. Chi-square test was applied after stratification of age, gender

duration of asthma marital status, residence, socio-economic status, employment status & history of psychiatric illness to evaluate the effect modification of frequency of depression by these variables. P value 0.05 considered as statistically significant.

RESULTS:

A total of 262 asthmatic teenager patients were included in this study with mean age + SD 55.49 + 11.67 years. Out of 262 patients, 93(35.5%) were male and 169(64.5%) were female. In this study out of 262 patients, 144 (55.0%) were from rural areas and remaining 118 (45.0%) were from urban areas. According to distribution of marital status 219 (83.5%) were unmarried and 43 (16.5%) were married. Out of 262 patients, 166(63.3%) belonged to poor class, 68(26.0%) patients belonged to middle class and 28(10.6%) belonged to upper

class of socio-economic status. Most of the patients i.e. 93(35.4%) were illiterate, 40(15.2%) were primary, 32(12.2%) were secondary, 48(18.2%) were matric pass and 49(19.0%) were intermediate. The mean duration + SD (range) of asthma was 5.6 + 1.32 (3 to 8 years). It was found that 30 (11.4%) cases had family history of asthma whereas 45(17.1%) cases had family history of depression. The total frequency of depression was found to be 37 (14.1%) among the teenagers.

In the present study it was observed that gender, Duration of asthma, residence, marital status, educational status, socio-economic status, history of psychiatric illness, employment status were significantly associated with depression (p value <0.05).

Figure 1: Frequency of Depression of the Patients (n=262)

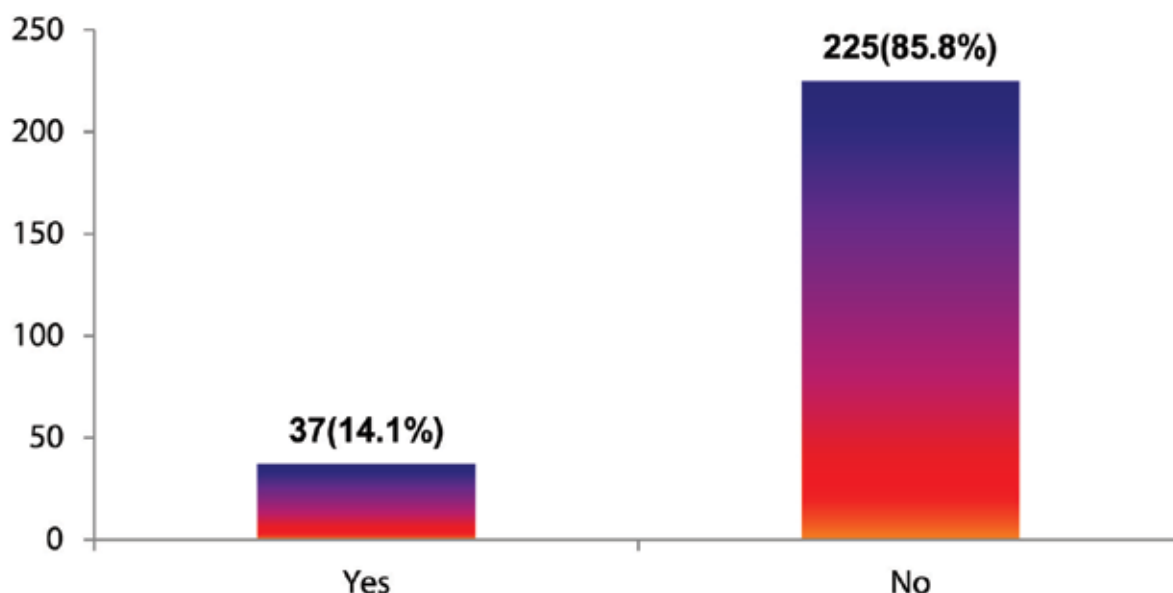


Table 1: Outcome of Depression with Mortality (n=262)

	With Depression (n=37)	Without Depression (n=225)	Total	p-value
Gender				
Male	29(78.4%)	64(28.4%)	93(35.5%)	<0.001*
Female	8(21.6%)	161(71.6%)	169(64.5%)	
Residence				
Rural	20(54.1%)	124(55.1%)	144(55.0%)	0.99
Urban	17(45.9%)	101(44.9%)	118(45.0%)	
Marital Status				
Single	19(51.4%)	200(88.9%)	219(83.6%)	<0.0001**
Married	18(48.6%)	25(11.1%)	43(16.4%)	
Educational Status				
Illiterate	25(67.6%)	68(30.2%)	93(35.5%)	<0.0001**
Primary	5(13.5%)	35(15.6%)	40(15.3%)	
Secondary	2(5.4%)	30(13.3%)	32(12.2%)	
Matric	2(5.4%)	44(19.6%)	46(17.6%)	
Intermediate	3(8.1%)	48(21.3%)	51(19.5%)	
Socio-Economic Status				
Poor	16(43.2%)	149(66.2%)	165(63.0%)	0.01*
Middle	17(45.9%)	51(22.7%)	68(26.0%)	
Upper	4(10.8%)	25(11.1%)	29(11.1%)	
History of Psychiatric Illness				
Yes	34(91.9%)	17(7.6%)	51(19.5%)	<0.0001**
No	3(8.1%)	208(92.4%)	211(80.5%)	
Employment Status				
Yes	10(27.0%)	100(44.4%)	110(42.0%)	0.04*

DISCUSSION

Our study results showed that individuals who have more depressive symptoms are having more respiratory problems in all the categories. A study of 700 individuals done by Janson and colleagues also shows the strong association between depression symptoms along with the worst respiratory status.⁽⁶⁾ Another two studies by Dales and Janson highlight powerful influence of psychological status of the patients with the self reported respiratory status. The conclusion of these both studies is to promote to evaluate the psychological status when individuals are reported with the respiratory symptoms. Neither of these studies assessed asthma in relation to depression.

In contrast, Yelloweas et al. assessed the psychological status in patients with severe

asthma. In this series of studies, the researchers found that around 33 to 40 % of psychiatrically diagnosed depression and anxiety have few groups of patients who had fatal attacks of asthma. They also reported that patients those have psychiatric issues have more prone to develop severe respiratory symptoms that effects their quality of life than that of those patients who do not have psychiatric issues.

According to the GDS scale for depression screening, the prevalence of depression symptoms in this current study is very high which is around 45% individuals enrolled from the primary care practice, considered positive for depression screening according to the GDS. The GDS, developed for the older aged patients but also showed validity for the younger patients, was chosen in this study because it is not subjected according to the confounding

effects related to the somatic complaints of the patients, which as shown above, are important when considering respiratory symptoms. Although GDS is excellent tool to screen the depression symptoms but it still does not help in case of diagnosis of major depression, which require fulfillment of psychiatric criteria.

In this current study, the diagnosis of depression was obtained by searching tool for appropriate ICD-9 codes in computerized charts. By using this method for establishment of the diagnosis of depression, we found that not majority of patients had an ICD-19 code for the diagnosis of major depression. Around 45% of patients had a screening for depression symptoms, when we used a GDS cut-off score 11. However 32% had positive screening when we used cut-off 14 which is similar to other studies that concluded that many patients were having positive screening for the depression symptoms even though they are not fulfilling the criteria for the diagnosis of major depression, rather have an milder form of affective syndrome.⁽⁷⁾

The prevalence of depression symptoms in the setting of primary care practice has also been studied by the others researchers. For example, an study had been done over the 1,900 primary care practice patients that screen for depression symptoms with the used of epidemiological studies depression scale. They found that the prevalence of depression related disorder is approximately around 22%.⁽⁸⁾ In another study, it was proved that 45% of the patients that are evaluated by a psychiatrist having depression symptoms that required anti depressant treatment.⁽⁹⁾ According to the recent reports by the consensus, depression is usually underreported by the majority of physicians for so many reasons and also been under diagnosed in general medical practice.⁽¹⁰⁻¹³⁾ As we did not confirm the diagnosis of depression by using comprehensive clinical criteria; even did not discuss the depression symptoms with physicians. For those reasons, we did not conclude that what is the actual prevalence rate of depression in our clinical

settings. However patients those who have higher GDS score were encouraged to speak about their depression symptoms to their physicians. In addition, physicians were also made aware about the high prevalence of depression symptoms in this sample during presentation of group results.

Many studies had also compared the association between depression symptoms to the asthma than those of control patients with or without pulmonary diseases. One study concluded that depression symptoms are higher in asthma patients as compared to the healthy individuals. Another study stated that depression symptoms are more prevalent in hospitalized patients with pulmonary diseases as compared to those who have an hospital admission for the other causes of pulmonary diseases.⁽¹⁵⁾ Although the precise nature of the association between depression symptoms and asthma is still not well known. Some researchers propose that same physiologic etiology, such as impairment of the voluntary activation of the diaphragm in depressed asthma patients, or have a cholinergic imbalance that link to related with the depression and smooth muscle bronchoconstriction. Some researchers also found correlations between higher depression symptoms and had a worse forced expiratory volume in 1 second (FEV1) and forced vital capacity⁽¹⁶⁾, while other researchers have concluded there is no correlation associated with the depressive symptoms and FEV1 or bronchial hyper responsiveness to methacholine challenge. Other researchers state that depression either is an independently coexisting with asthma or as related due to the drugs that are used to treat asthma.^(2, 4) Alternatively, it can be possible that asthma patients have poor quality of life (psychical inactivity related to precipitating symptoms), which is turn can contribute the depression.^(2,4) Because the current study design of our study is cross sectional, cross- directionality or a causal relation between depression and asthma symptoms cannot be proved from our results.

The current study has many limitations as well. First, limited numbers of the patients scheduled for the physicians who did not have severe co-morbidities as health-related quality of life and depression symptoms may be different in these patients compared with enrolled patients. Also, our study enrolled patients from the diverse socio-demographic groups, which are eventually not possible to generalize our finding to the all socio-demographic groups. Second, assessment of current asthma activity were measured with the self report of the patients performance based measures, such as used of peak flow meter may helps to provide standardized approach to the asthma patients. Third, the GDS were originally designed for the self-administered questionnaire. In our study, the GDS was administered during in-person interviews that may affect the way patients may respond to the physicians. Also, while the GDS has been previously tested in younger individuals, but in our knowledge it has not been used in individuals as young as in our current study. Fourth, although the GDS is an excellent screen for depression, we did not formally diagnose depression as part of this study. Finally, we also did not measure the status of others psychological states, especially anxiety, which have been coexisting with depression in asthma patients.

The current study results showed that depression symptoms among the asthma patient are more common and had an poor performance status along with poor quality of life than that of those who are without the depression symptoms in asthma patients. Whether this is due to depressed patients being more likely to report worse respiratory status or an intrinsic underlying relation between depression and asthma is not known. However, given the current emphasis on functional status and health-related quality of life measured by disease-specific and general health scales, we conclude that psychological status indicators should be considered when patient-derived measures are used to assess outcomes in patients with asthma.

CONCLUSION

This study concluded that depression is more prevalent among the teenager patients with asthma. Much evidence from the previous studies suggests that these disorders frequently co-occur. It is important for future studies to document the extent of co-morbidity and whether co-morbid anxiety disorders are associated with decreased self-efficacy and self-care, higher symptom burden, decreased functioning, and increased medical costs. A greater understanding of teenage usage will affect their adherence by improving both communication and attitudes towards treatment, therefore keeping asthma under control. A further relation between asthma and central nervous system is suggested

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COMPARATIVE ANALYSIS OF IMMUNOCHROMATOGRAPHIC DIAGNOSTIC TEST AND MICROSCOPY FOR THE DETECTION OF PLASMODIUM SPECIES

¹Shahzad Ali Jiskani, ¹Saira Rajput, ¹Umair Ali Soomro, ²Sikandar Ali Bhand

¹Department of Pathology, Indus Medical College Tando Muhammad Khan

²Department of Paediatrics, Indus Medical College Hospital, Tando Muhammad Khan

Corresponding Author:

Shahzad Ali Jiskani

MBBS, M.Phil (Haematology)

Senior Lecturer, Department of Pathology

Indus Medical College, Tando Muhammad Khan

Co-Authors:

Saira Rajput

BS (Biochemistry)

Medical Laboratory Technologist, Pathology

Laboratory

Indus Medical College, Tando Muhammad Khan

Umair Ali Soomro

MBBS, M.Phil (Haematology)

Assist. Professor, Department of Pathology

Indus Medical College Tando Muhammad Khan

Sikandar Ali Bhand

MBBS, FCPS (Paediatrics)

Associate Professor, Department of Paediatrics,

Indus Medical College Hospital Tando Muhammad Khan

Corresponding author email:

shahzadbaloach289@gmail.com

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Abstract

INTRODUCTION: Light and thin film microscopy is a cost-effective gold standard for Malaria diagnosis is time consuming but needs expertise. In detecting Plasmodium species, immunochromatographic technique (ICT) has been claimed as an alternative to light microscopy.

OBJECTIVE: This research was performed in reference to light microscopy of the smears to determine sensitivity and specificity of rapid malaria testing.

PATIENTS AND METHODS: This study was carried out between January and September 2018 at Department of Pathology, Indus Medical College Hospital Tando Muhammad Khan. 105 patients with an evocative history of malaria were subjected to both tests, i.e. light microscopy and Immunochromatographic Technique (ICT) malaria P.f./Pan Rapid Test System for two methods comparison.

RESULTS: The findings of the blood test showed that 49 patients (46.66%) were infected with malaria and the remaining 47 (44.76%) were negative for malaria. *P.falciparum* was found in 17 of positive patients. In the remaining 32 cases (65.30%) non-falciparum plasmodium species were found. The findings of the P.f./Pan ICT malaria test showed that 47 (44.76%) of the patient samples were positive for malaria parasites and 58 (55.23%) were negative for malaria parasites. 16 cases (32.65%) of *P. falciparum* infection and cases of non-falciparum plasmodium species accounted for

remainder of the 31 cases (63.26%). ICT malaria therefore showed 94.25 per cent sensitivity and 95.00 per cent specificity for malaria parasite detection.

CONCLUSION: Immunochromatographic technique offers user-friendly, accurate, sensitive alternative to slide microscopy for malaria diagnosis without adding cost and effort.

KEYWORDS: Malaria, Plasmodium, Immunochromatography, Microscopy, Thick and thin

Citation:

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films, Diagnostic Test, Sensitivity, Specificity.

INTRODUCTION:

Malaria is one of the most dangerous infectious parasites. It infects about 200 million people worldwide and annually kills around 2 million people because of malaria. ⁽¹⁾ A prompt and accurate diagnosis is the first step towards effective malaria treatment. Several laboratory procedures have been developed for malaria diagnosis, such as routine light microscopy, immunological methods for antigen detection, polymerase chain reaction, specie-specific DNA test method and ribosomal RNA method. ⁽²⁾ Thick and thin films are among these the most commonly used tool for demonstration of plasmodium organisms. This method is regarded as a gold standard since it is relatively simple and cheap. ⁽³⁻⁵⁾ But the hassle of routine microscopy is time consuming, requires considerable expertise and its reliability is questionable when parasitemia levels are low. ^(1, 6)

Immunochromatography (ICT) is one of the recently developed techniques for rapid malaria diagnosis. ⁽¹⁾ This approach is focused on the identification of malarial antigen, released from parasitized cells. This is a modern technique designed for circumstances where there is no accurate microscopy. ⁽⁷⁾ Malarial disease ICT detected antigens include histidin-rich proteins-2 (HRP-2), plasmodium LDH, and plasmodium aldolase. ⁽⁸⁻⁹⁾ Dipstick type kits are available commercially for malaria antigen detection with excellent sensitivity and specificity. ⁽¹⁾

This study was performed in reference to traditional light microscopy to determine sensitivity and specificity of the rapid malaria test.

PATIENTS AND METHODS

This study was carried out between January and september 2018 at Department of Pathology, Indus Medical College Tando Muhammad Khan. The study included 105 patients of all ages and

sexes with history of high-grade fever associated with chills and rigours, as well as other non-specific symptoms such as generalised body aches, exhaustion and abdominal discomfort. The study excluded patients who received any antimalarial medication or had some other known cause of fever and critically ill patients. Venous blood from each patient was collected into a sterile vial containing anticoagulant EDTA.

Blood films of thick and thin smear were prepared and stained with Wright's technique. Two light-microscope microscopists independently tested both slides for malaria parasites. A thin smear of the blood was analysed for 15 minutes and 200 fields were visualised for a dense blood smear. Results were analyzed.

P.f./Pan Rapid Test System developed by ABON PLUS Biopharm (Hangzhou) Co. Blood samples were tested with ICT malaria. Ltd. It is a qualitative membrane-bound test for plasmodium falciparum, plasmodium vivax, plasmodium ovale and plasmodium malariae detection. For identification of other three plasmodium species, the membrane is precoated with anti-HRP 2 specific antibodies for plasmodium falciparum and plasmodium specific anti-aldolase anticorps. Testing was carried out as per the instructions of the manufacturer.

Interpreting the findings of the test as follows:

- i) P. falciparum test was considered positive if one line appears in the control region and one in the particular region of plasmodium falciparum
- ii) Test was considered as a particular positive species of non-falciparum plasmodium if one line appears in the control region and one in the pan malarial region
- iii) Testing was known as a mixed infection if one line occurs in the control area, one in the plasmodium falciparum area and one in the pan malarial region

iv) Tests is deemed negative if only one line appears in the control region

RESULTS

The ICT malaria P.f / Pan test device and the light microscopy were used to screen a total of 105 blood samples for malarial parasites, and the results were compared. Results from the blood film showed that 49 (46.66%) patients were infected with malaria, and the remaining 56 (53.33%) were negative. *P. falciparum* were detected in 17 cases (34.69%) and the non-*falciparum* plasmodium species were detected

in the remaining 32 cases (65.30%). In none of them is mixed infection. Accordingly, the results of the P.f./Pan ICT malaria test showed that 47 (44.76%) of the patient samples were positive for malaria parasites and 58 (55.23%) were negative for malaria parasites. *P. falciparum* infection accounted for 16 cases (32.65%) and the remaining 31 (63.26%) cases were non-*falciparum* plasmodium types. In none of the cases, mixed infection is detected again.

Table 1: Rate of detection of malaria parasite by different methods (n=105)

Test	Results	
	Positive	Negative
Peripheral blood film (n=105)	49 (46.66%)	56 (53.33%)
ICT method (n=105)	47 (44.76%)	58 (55.23%)

Table 2: Evaluation of ICT as diagnostic test for malaria parasite (n=105)

Test (ICT)	Malaria Parasite		Total
	Present	Absent	
Positive	45 = a	02 = c	47 = a+c
Negative	02 = b	56 = d	58 = b+d
Total	47 = a+b	58 = c+d	105

a = True positive

b = False negative

c = False positive

d = True negative

$$\text{Sensitivity} = \frac{a}{a+b}$$

$$\text{Specificity} = \frac{d}{c+d}$$

Considering microscopy as the gold standard for malaria parasite diagnosis, the current study finds ICT malaria sensitivity and specificity as high as 94.25 per cent (95 per cent confidence interval: 78.92 – 99.12) and 95.00 per cent (95 per cent confidence interval: 84.01 – 99.17) respectively.

DISCUSSION

Even though the gold standard for malaria diagnosis remains microscopy, there are still a range of restrictions, such as the lack of qualified microscopists, time consuming for microscopy. Particularly in countries like Pakistan with endemic malaria, huge population and scarcity of trained microscopists, an easily performed, quick, and accurate test for the detection of plasmodial infections is required. Immunochromatographic technique (ICT) offers an incentive for early detection of malaria in the course of disease and encourages effective treatment in patients with malaria, thus decreasing mortality.⁽¹⁰⁻¹³⁾

The current study was conducted to compare

ICT with the microscopic method of detecting malarial parasites and to determine the diagnostic accuracy (sensitivity and specificity) of the ICT system by considering microscopy as the standard gold. The findings showed 93.75 (95 percent trust interval: 79.19 – 99.23) percent sensitivity and 95.00 (95 percent trust interval: 83.08 – 99.39) percent specificity. These results are consistent with many related studies carried out within and outside Pakistan. Findings from a number of related studies are listed below. Jan Mohammad et al. demonstrated that for malaria, ICT yielded very high sensitivity (96.1 percent) and specificity (95.7 per cent). Also very poor were the false positive rates and false negative rates, 4.3 per cent and 3.9 per cent respectively.

⁽¹⁴⁾ Under Zareen Fasih et al. Extremely specific ICT approach was found (91 per cent) and 85 per cent vulnerable to malaria detection in infants. ICT's positive predictive value (PPV) is 68%. ICT's negative predictive value (NPV) is 96%. ⁽¹⁵⁾ Jahan Zeb and his colleagues used two rapid test methods, i.e. ICT and OptiMAL instruments, which showed 100% sensitivity and specificity for *P.falciparum* and 75 to 87.5% sensitivity and 100% specificity for *P.vivax*. ⁽¹⁶⁾ Mahadev Harani also found similar results, i.e. in his analysis, ICT was 97.0 percent sensitive for *P.falciparum*, 98.3 percent precise, 78.0 percent positive predictive value (PPV) and 99.8 percent negative predictive value (NPV). The sensitivity for *P.vivax* was just 89.7 percent, 97.9 percent specificity, 70.3 percent PPV and 99.4 percent NPV. ⁽¹⁾ Sheik S et al found that, compared with standard microscopy, rapid diagnostic tests (RDTs) had the same sensitivity and specificity. Sensitivity, concreteness Positive predictive value and negative predictive value of RDT were 95%, 91.6%, 0.55% and 99.3% respectively. ⁽¹⁷⁾ Batwala V et al found that the sensitivity of presumptive diagnosis based on axillary temperature, microscopy of the health centre and rapid diagnostic testing was: 42.6%, 85.1% and 97.9% respectively. The corresponding specificity rates were found to be 73.1 percent, 93.7 percent and 74.7 percent respectively, resulting in superior sensitivity compared to

microscopy being shown by malarial antigen-based experiments. ⁽¹⁸⁾

Considering consistent results from all of these studies in favour of fast, easy-to-perform, responsive and accurate ICT testing and taking into account the prevalence and complexity of malaria disease and the rapid spread of antimalarial drug resistance in Pakistan, it would be advantageous to consider ICT as an agreed standard for diagnosing malaria parasite. ⁽¹⁹⁻²¹⁾

CONCLUSION

It is concluded that the technique of immunochromatography provides a sensitive, specific, user-friendly and practical alternative to slide microscopy for malaria diagnosis without adding cost and effort.

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MATERNAL THYROID STATUS AND ITS ASSOCIATION WITH IRON PROFILE

¹Arshad Ali Lakho, ¹Zahida Zia, ²Sher Ali, ³Mubashir Raza, ⁴Ashraf Ali

¹Polyclinic Hospital, Islamabad, ²Shifa International Hospital, Islamabad

³Pakistan Institute of Medical Sciences, Islamabad, ⁴Health Services Academy, Islamabad

Corresponding Author:

Arshad Ali Lakho, FCPS (Paediatrics)
Senior Registrar, Department of
Paediatrics, Polyclinic Hospital Islamabad

Co-Authors:

Zahida Zia
FCPS (Gynecology & Obstetrics)
Consultant Gynaecologist, Department of
Gynaecology and Obstetrics,
Polyclinic Hospital Islamabad

Sher Ali, FCPS (Medicine)
Senior Medical Officer, Department of
Medicine, Shifa International Hospital
Islamabad

Mubashir Raza
Postgraduate Resident, Department of
Paediatrics, Pakistan Institute of Medical
Sciences, Islamabad

Ashraf Ali, MPH
District Surveillance Officer,
Health Services Academy, Islamabad

Corresponding Author Email:
arshad.lakho34@yahoo.com

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were hyperthyroid, 35 (39.77 percent) were hypothyroid in iron-deficient pregnant women, 29 (32.95 percent) were euthyroid and 24 (27.77 percent) were hyperthyroid. The thyroid status difference was statistically significant in both groups ($p < 0.001$).

CONCLUSION: Iron deficiency has been closely linked to deranged thyroid status. Thus, iron therapy is required to retain status as both have effects on one another.

ABSTRACT

INTRODUCTION: Iron deficiency anemia is very common during pregnancy, and is associated with increased foetal demand and use. Iron plays an important role in our body, influencing many physiological functions including the function of thyroid.

PATIENTS AND MATERIALS: This is a cross sectional study conducted at Polyclinic Hospital Islamabad and was performed during 6 months period (December 2017 to July 2018). 88 pregnant females with iron deficiency anemia and 90 normal control of pregnancy females with normal iron status and no anemia were included in the study. All were evaluated for detection of hemoglobin, serum ferritin and thyroid profile. P – value of < 0.05 was considered as statistically significant.

RESULTS: The mean patient age was 25.24 ± 3.1 years for normal pregnant women and 26.21 ± 3.5 years for iron-deficient pregnant women. The mean gestational age was 29.39 ± 2.1 weeks in normal pregnant women and 28.18 ± 2.7 weeks in iron deficient pregnant women. 5 (5.55 percent) were hypothyroid in normal pregnant women, 83 (92.22 percent) were euthyroid and 2 (2.22 percent)

KEYWORDS: Iron deficiency anemia, thyroid function, iron profile, pregnancy.

INTRODUCTION

Iron deficiency anemia is the most common nutritional deficiency of all problems with micronutrients. Iron deficiency has many detrimental effects in all age groups. It reduces the ability and performance of work in older children and adults, and disturbs the immune system. It also has to do with reduced

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reproductive ability. Iron deficiency shows effects on heme – based enzymes that result in several functional failures. Iron deficiency, which is more prevalent during gestation due to increased use of iron, causes more issues in relation to other age groups.⁽¹⁾ Pregnancy has clear effects on thyroid hormones and their function. Thyroid gland shows 10 percent enlargement during pregnancy in iodine – stuffed countries and 20 – 40 percent in areas with iron insufficiency. In addition to increased daily demand for iodine, the production of triiodothyronine (T3) and thyroxine (T4) also rises by 50 percent. There is also a marked increase in thyroxin – binding globulin (TBG) due to thyroxin stimulation – binding globulin (TBG) production through increased maternal oestrogen levels and decreased liver clearance due to oestrogen-induced sialylation. This would result in a rise in the extra thyroid reservoir, eventually leading to an increase in total concentrations of T3 and T4.⁽²⁾ These changes can cause hypothyroidism in later part of pregnancy in iodine-deficient females.⁽³⁾ Iron deficiency can disrupt thyroid hormone synthesis by decreasing plasma concentrations T3 and T4 due to impairment of two initial steps that are catalysed by the enzyme heme-dependent thyroid peroxidase (TPO) in the thyroid hormone synthesis. There is also a decreased response of TSH to TRH, reduced peripheral conversion of T4 to T3 and increased circulation of TSH.⁽⁴⁾

This study helps imagine the association between iron deficiency during pregnancy and

thyroid hormone maternal status.

PATIENTS AND METHODS

This is a cross-sectional analysis conducted during the period January 2017 to July 2018 at the Polyclinic Hospital Islamabad. A total of 178 patients were chosen for the study that included iron deficiency anemia in pregnant women and normal pregnant control. 90 patients were taken as controls which included pregnant women without anemia with iron deficiency. In both classes, the age ranged from 20 to 40 years. All patients with history of the medication, sepsis, diabetes mellitus, hypertension, iron supplementation history or documented thyroid disorder were excluded from the study. Criteria were developed for explaining anemia with iron deficiency. A serum ferritin concentration of less than 20 µg/L and a hemoglobin concentration of less than 11 g/dL are considered anemia with an iron deficiency. Blood samples were taken from all patients into two tubes. The serum TSH, T3, and fT4 samples obtained in Gel tube were evaluated. The thyroid disorder was graded according to the guidelines of the American Thyroid Association. It involves hypothyroidism (increased TSH along with reduced fT4), subclinical hypothyroidism (increased TSH alongside normal fT4), hyperthyroidism (reduced TSH along with increased fT4), and subclinical hyperthyroidism (reduced TSH along with normal fT4);.

Data were analyzed and evaluated using SPSS version 21.0. P – value of <0.05 was considered statistically significant.

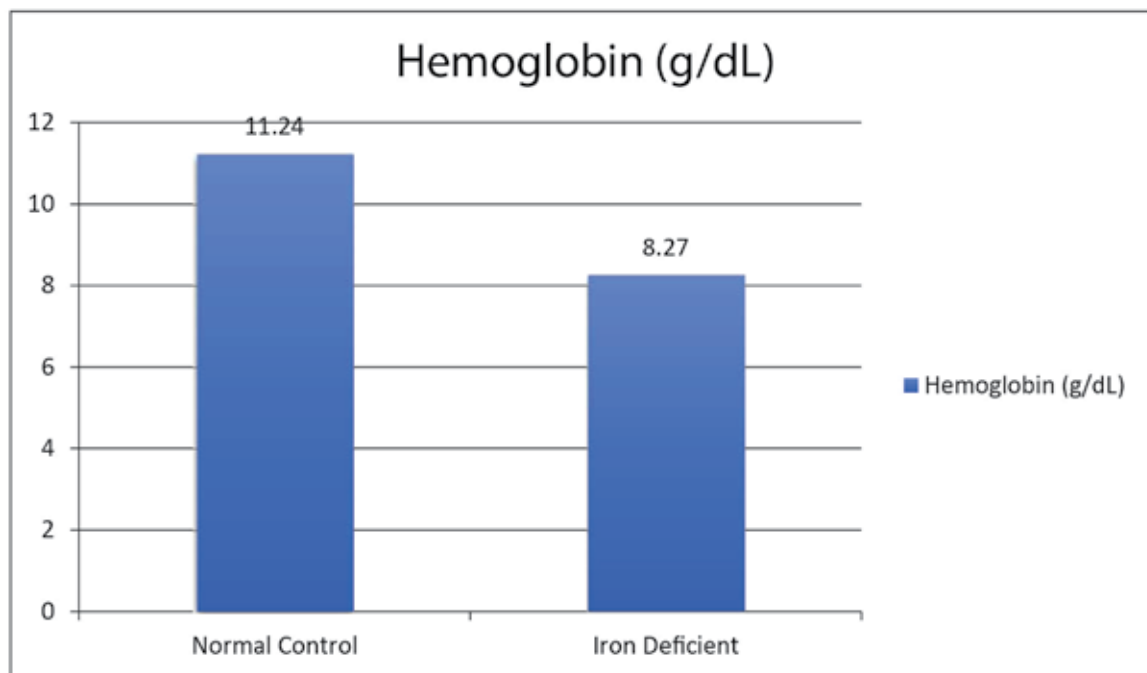
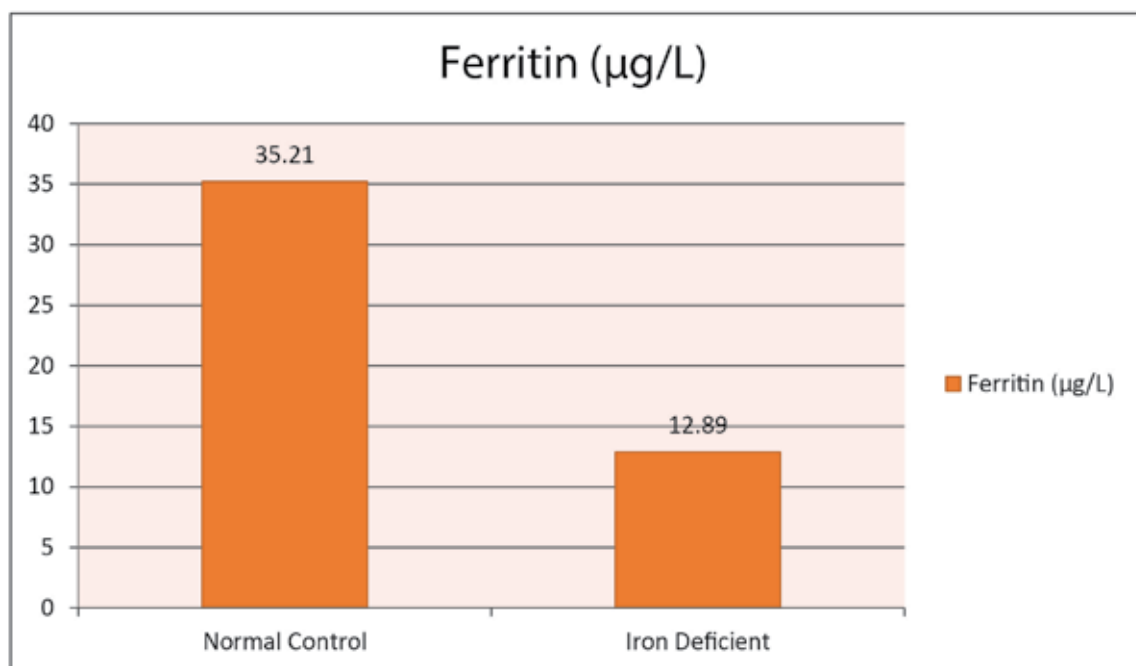
RESULTS

Table 1: Baseline parameters in both groups (n=178)

	Normal pregnancy females (n = 90)	Iron – deficient pregnant females (n = 80)
Mean age (years)	25.24 ± 3.1	26.21 ± 3.5
Mean gestational period (weeks)	29.39 ± 2.1	28.18 ± 2.7
Mean hemoglobin levels (g/dL)	11.24 ± 1.57	8.27 ± 1.09
Mean serum ferritin levels (µg/L)	35.21 ± 2.16	12.89 ± 4.21

Table 2: Thyroid status in both groups (n=178)

Status	Normal Pregnant Patients (n=90)	Iron – Deficient Pregnant Patients (n=88)	P – value
Hypothyroid	5	35	<0.001
Euthyroid	83	29	<0.001
Hyperthyroidism	2	24	<0.001

**Figure 1: Hemoglobin difference in both groups (n=178)****Figure 2: Ferritin difference in both groups (n=178)**

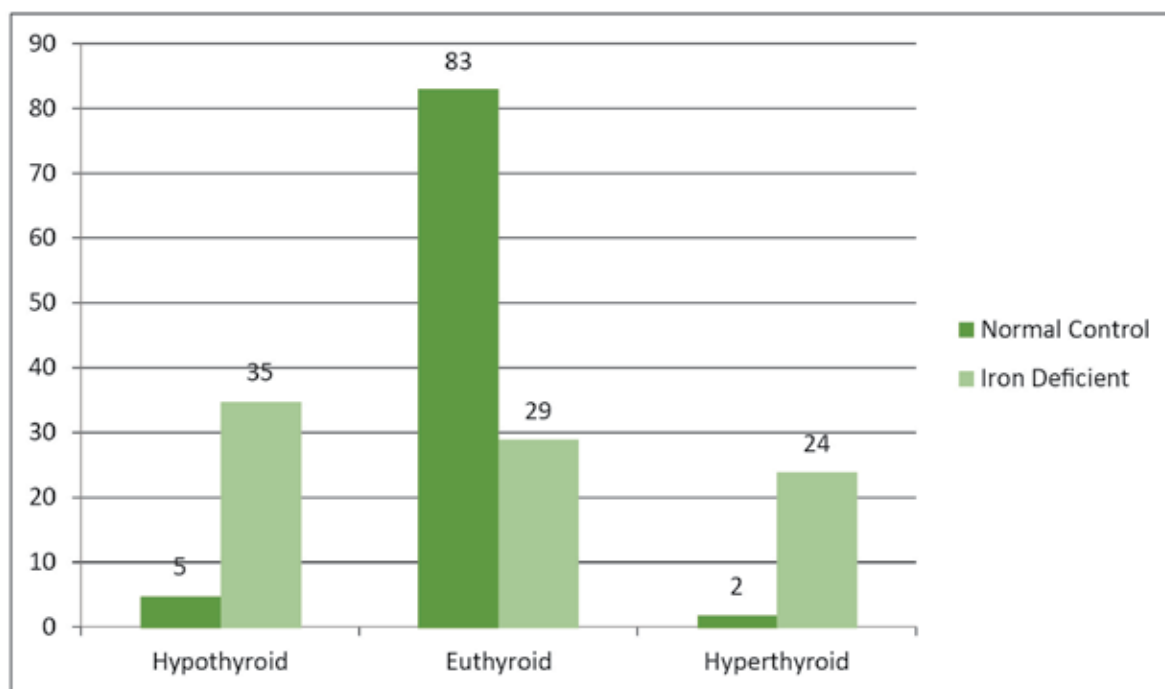


Figure 3: Thyroid status in both groups (n=178)

DISCUSSION

Iron deficiency is recognized as a common public issue with a high prevalence and affects about 2 billion people worldwide.⁽⁵⁾ Pregnant females are more vulnerable to iron deficiency because of increased foetal demand. Iron is an essential micronutrient to our body, and its lack causes many physiological and metabolic reactions to alter. Iron deficiency leads to numerous issues including disruption of cognitive function, behavioral changes, immunity deficits, issues with thermoregulation and decreased work ability.⁽⁶⁾ Furthermore, iron deficiency anemia is a serious consequence of iron deficiency and is the most common form of anemia.⁽⁷⁾ Abundant and compelling clinical evidence indicated that iron deficiency anemia during pregnancy is associated with a wide range of perinatal and maternal hazardous consequences including premature birth, low foetal birth weight and impaired foetal neurological growth. It is also clear that iron stores in neonates can be impaired when mom suffers from anemia with iron deficiency.⁽⁸⁾ It is now also postulated that iron deficiency with or without anemia influences thyroid metabolism. It decreases plasma levels T3 and T4, decreases the peripheral conversion of T4 to T3, and raises plasma TSH concentration.⁽²⁾

Thus Iron deficiency is a likely factor in endemic goiter growth. The exact process, however, isn't clear. Iron deficiency is responsible for thyroid metabolism derangement by influencing and altering the typical hypothalamic – pituitary – thyroid (HPT) axis, thereby decreasing the adherence of T3 to hepatic nuclear receptors or probably due to anemia and reduced oxygen transport.⁽⁹⁾ Iron deficiency affects even T4's hepatic function.⁽⁵⁾

Deiodinase, the enzyme responsible for the conversion of T4 into T3 or the thyroid peroxidase function responsible for the synthesis of thyroid development, as it is iron – based on.⁽¹⁰⁾ Meanwhile iron therapy supplementation restores thyroid function. Some intervention studies have been performed and have shown that iron supplementation significantly improves the efficiency of iodized oil and salts in pediatric goiter patients. Iron therapy in females with subclinical hypothyroidism also demonstrated a modest increase of T4 and a small decrease in TSH. Hypothyroidism itself, however, is also responsible for numerous hematological defects, as different pathways are involved in developing these problems. Iron deficiency anemia may be due to low bowel absorption combined with thyroid hormone

deficiency or the related gastric achlorhydria. So thyroxine supplementation is very necessary. (6,11)

In the present study it was postulated that in pregnant women with iron deficiency thyroid status was deranged. The levels of hemoglobin and ferritin in both classes of iron were substantially different (Table 1, figure 1 and 2). Most iron-deficiency anemia patients were associated with hypothyroidism, accompanied by euthyroid. Though very limited percentage of patients in normal control group had skewed thyroid status (Table 2, figure 3). In both groups there was a statistically significant difference in parameters, which indicates a possible association between iron deficiency and thyroid status.

CONCLUSION

The iron deficiency has been closely linked with deranged thyroid hormone functions in current research. Proper diagnosis and treatment is therefore very necessary to resolve this deficiency, as it can cause adverse effects on both mother and foetus.

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STUDY ON RELATIONSHIP BETWEEN HYPERURICEMIA AND DYSLIPIDEMIA

¹Ramesh Kumar Suthar, ²Kavita Bai, ²Mumtaz Ali Memon, ³Keenjhar Rani

¹Department of Medicine, Indus Medical College, Tando Muhammad Khan

²Department of Physiology, Indus Medical College, Tando Muhammad Khan

³Department of Physiology, Liaquat University of Medical and Health Sciences, Jamshoro

Corresponding Author:

Ramesh Kumar Suthar

MD (General Medicine)

Assistant Professor of Medicine

Indus Medical College TMK

Co-Authors:

Kavita Bai, M. Phil (Physiology)

Assistant Professor of Physiology

Indus Medical College TMK

Mumtaz Ali Memon, M. Phil (Physiology)

Professor of Physiology

Indus Medical College TMK

Keenjhar Rani, M. Phil (Physiology)

Assistant professor Physiology

Liaquat University of Medical and Health Sciences, Jamshoro

Corresponding author email:

rk22258627@gmail.com

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Abstract

OBJECTIVE: To evaluate the correlation between high serum uric acid levels and lipid profile so as to yield dynamic precautionary actions from emerging imminent cardiovascular ailments.

METHODOLOGY: This research study was piloted on 180 adult patients (n=180), 90 hyperuricemic and 90 healthy controls in the Department of Medicine and Physiology, Indus Medical College Tando Muhammad Khan, and the duration of study was six months (from April 2018 to July 2018). Patients who were alcoholic, having diagnosis of chronic hepatic illness, renal conditions, cardiovascular diseases as well as those taking lipid lowering agents and on the treatments that can disturb uric acid were disqualified from this research

study. Lipid profile performed for those who found with raised uric acid levels but without symptoms and those presented with gout. Data catered and evaluated on SPSS version 16.0. Quantitative factors were uttered as mean + standard deviation. To compare the means, student t test was applied. Positive and negative correlation was likewise calculated through regression analysis.

RESULTS: This research study revealed significant results with positive association ($p < 0.05$) between uric acid and total cholesterol, triglycerides and low density lipoprotein. Instead, remarkable negative association observed between uric acid and high density

lipoprotein levels (p value < 0.05).

CONCLUSION: Hyperuricemia is linked with dyslipidemia that may lead to imminent cardiovascular conditions. Consequently, cardiovascular emergencies can be possibly prevented by diagnosing as well as timely managing in elevated uric acid level and dyslipidemia.

KEYWORDS: Hyperuricemia, dyslipidemia, high density lipoprotein, triglycerides.

INTRODUCTION

Hyperuricemia is an ailment that upshots from either augmented production or a bridged

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elimination of uric acid otherwise combination together. As a product of purine degradation, uric acid is generated as the end concern among humans.^(1,2) Current preclinical as well as clinical demonstrations proposes that chronically raised uric acid levels are self-governing threat element for hypertension including cardiovascular ailments, chronic kidney disease, type 2 diabetes mellitus as well as cognitive drop and raised arterial pressure.^(2,3) Among adults if serum uric acid levels, found to be greater than 7.0 mg/dL and 6.0 mg/dl among male and female gender respectively; then those individuals will be demarcated as hyperuricemic.^(4,5) Hyperuricemia has lately appeared as self-governing possibility aspect in the expansion to type 2 diabetes mellitus as well as hypertension through numerous projected ways and both found to be imperious communal health encounters with direct proportion of amplified risk of cardiovascular occasions. Insufficient clinical trial based studies has examined the usage of uric acid depressing agents in managing such affected individuals; though, some of their outcomes provided hopeful indication to a prospective role for such agents in combating disease burden.⁽⁵⁾ Latest research submits that hyperuricemia might be possibly originated by upraised activity of the enzyme xanthine oxidase.⁽⁶⁾ On of the research project report that raised plasma uric acid level, somewhat concealed from the deteriorating heart, is a prognostic interpreter among those suffering from congestive cardiac failure.⁽⁷⁾ Hyperuricemia induces renal inflammation, endothelial dysfunction and so, steadily stimulates renin-angiotensin system that may lead to hypertension and chronic kidney disease. A small number of clinical trials had also measured the use of uric acid-lowering treatments i.e., allopurinol and febuxostat in managing such cases.⁽⁸⁾ This way, correlation of uric acid levels with cardiovascular accidents has become complicated to govern whether uric acid has a contributory role in these conditions or raised uric acid is just an indicator for persons at augmented risk, replicating the relationship by means of additional risk

factors i.e., dyslipidemia, metabolic syndrome and diabetes mellitus.⁽⁹⁾ There are numerous epidemiological studies that propose the association of cardiovascular diseases and uric acid.⁽¹⁰⁻¹⁴⁾ but very few studies highlight the direct association of hyperuricemia with lipid profile; so the affiliation of dyslipidemia amongst persons with hyperuricemia remain to be principally not well-measured.

Using this contextual the current study was directed to assess the lipid profile among the individuals with elevated uric acid concentration in our populace. Subsequently taking dynamic preventive measures can hinder the progression to cardiovascular disease (CVD) and also incidence of other co morbidities.

METHODOLOGY

This research study was piloted on 180 adult patients (n=180), 90 hyperuricemic and 90 healthy controls in the Department of Medicine and Physiology, Indus Medical College Tando Muhammad Khan, and the duration of study was six months (from April 2018 to July 2018). Total 90 patients (n=90) including male and female patients with symptoms of Gout / asymptomatic increased uric acid level and 90 normal healthy controls (n=90) meeting the selection criteria were recruited for this research study. Study conducted after approval from institutional ethical committee and taking informed consent from study participants. A group of 90 patients (n=90) including male and female with asymptomatic hyperuricemia individuals / gout patients of 20 – 60 years were included for this study. Normal healthy age and gender matched individuals (n=90) were included as normal controls. Patients who were alcoholic, having diagnosis of chronic hepatic illness, renal conditions, cardiovascular diseases as well as those taking lipid lowering agents and on the treatments that can disturb uric acid were disqualified from this research study.

After all aseptic measures, 12 hours fasting intravenous blood sample taken to investigate for fasting blood sugar, serum creatinine, serum urea, serum uric acid and lipid profile. Serum

creatinine and urea measured to exclude renal dysfunctions. Serum/plasma urea 2.5-7.8 mmol/L is representative of normal glomerular filtration rate.⁽¹⁵⁾ Serum creatinine levels 0.72–1.18mg/dl in men and 0.55–1.02mg/dl in women considered normal.⁽¹⁶⁾ Dyslipidemia denotes the augmented levels of total cholesterol, raised triglycerides and LDL with or without reduced HDL. A combination of lipid abnormalities, hypertriglyceridemia and low HDL, stand metabolically interlinked and ought to be labeled as atherogenic dyslipidemia.⁽¹⁷⁾

Blood pressure measured at three equal intervals repeatedly on the right arm with mercury aneroid sphygmomanometer, study participants being in a quiet sitting position afterwards at least 05 minutes of rest to exclude hypertension. When the systolic arterial pressure was ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/ or individual was taking antihypertensive medication were demarcated as hypertensive.⁽¹⁶⁾

Data catered and evaluated on SPSS version 16.0. Numerical factors were uttered as mean \pm standard deviation. To compare the means, student t test was applied. Positive and negative correlation was likewise calculated through regression analysis.

RESULTS

Among 180 participants (n=180), with 90 subjects in healthy control group were 27

(15%) males and 63 (35%) females. While in the hyperuricemia group out of 90 high serum uric acid patients 48(26.67%) were male and 42(23.33%) females (Figure No. 1). Mean serum uric acid (mg/dl) in hyperuricemia patient group and healthy control group were 7.6 ± 0.63 and 4.3 ± 0.45 respectively (Table No. 1). Lipid profile compared among hyperuricemia group and healthy controls by applying independent t- test. Total cholesterol, triglycerides, HDL and LDL levels among hyperuricemia group Vs healthy control were 17.33 ± 31.7 Vs 160.54 ± 32 (p value=0.008), 161.37 ± 36.2 Vs 127.72 ± 26.3 mg/dL (p value <0.01), 27.51 ± 2.6 Vs 39.12 ± 3.7 mg/dL (p value <0.01), and 124.65 ± 12.5 Vs 99.56 ± 23.2 mg/dL (p value <0.01) respectively (Table No. 2). Serum uric acid, total cholesterol, triglycerides, HDL and LDL correlated by applying bivariate analysis Pearson correlation (Table No.3). Total cholesterol, triglycerides and LDL are positively correlated with uric acid (r value =0.19, 0.49 and 0.45 respectively) while HDL levels are negatively correlated with uric acid (r value -0.887).

Table 1: Mean serum uric acid (mg/dl) between hyperuricemia patient group and healthy control group (n = 180)

Study participants	Serum Uric acid (mg/dL)	P-value
Hyperuricemia group (n = 90)	7.6 ± 0.63	<0.01
Healthy Control group(n = 90)	4.3 ± 0.45	

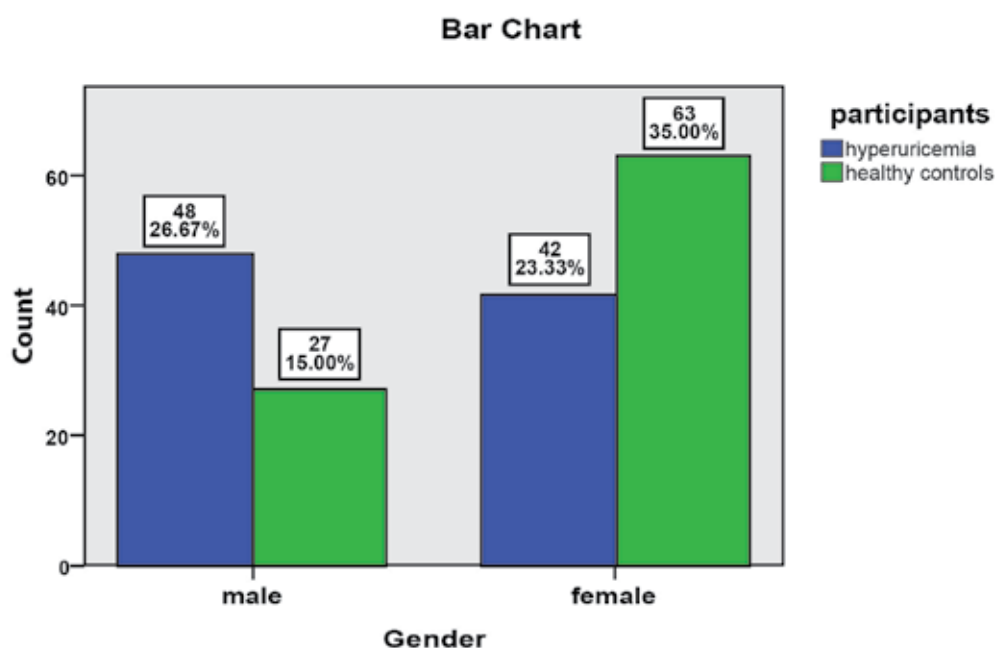


Figure no. 1: Gender based distribution of study population (n=180)

Table No. 2: Lipid Profile among hyperuricemia patients and healthy controls (n=180)

Group Statistics					
	Study participants	N	Mean	Std. Deviation	P value
Totalcholesterol (mg/dl)	hyperuricemia	90	173.33	31.787	0.008**
	healthy controls	90	160.54	32.076	
Triglycerides(mg/dl)	hyperuricemia	90	161.37	36.250	0.00**
	healthy controls	90	127.72	26.352	
HDL(mg/dl)	hyperuricemia	90	27.51	2.644	0.00**
	healthy controls	90	39.12	3.770	
LDL(mg/dl)	hyperuricemia	90	124.65	12.521	0.00**
	healthy controls	90	99.56	23.269	

Table No. 3: Bivariate analysis of serum uric acid (n=180)

		Total cholesterol(mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL(mg/dl)
Serum uric acid (mg/dl)	r-value	.191*	.497**	-.887**	.456**
	p-value	.010	.000	.000	.000
	N	180	180	180	180

*Correlation is significant at the 0.05 level.

**Correlation is significant at the 0.01 level.

DISCUSSION

This study conceded out to prove whether hyperuricemia with absence of known cardiovascular ailment is allied with dyslipidemia, consequently, knowing and managing such person may avert expansion to cardiovascular dysfunctions. This research study has revealed the strong relation of raised uric acid levels with variations in lipid profile similar to study by Peng TC et al.⁽¹⁸⁾, Lippi et al.⁽²⁶⁾ and Sarmah D et al.⁽⁹⁾ who also concluded that both, hyperuricemia and dyslipidemia are inter related and may predispose such people to future cardiovascular events. Thus managing such hyperuricemic people timely may condense cardiovascular morbidity. Dyslipidemia is an imperative possibility factor to develop coronary artery disease as well as stroke. Many potential epidemiologic research studies have consistently revealed that people living in good health lifestyles as well as those with promising lipid profiles, have curtailed incidence of coronary heart disease. Anticipation and management of dyslipidemia can distinctly modify cardiovascular morbidity plus mortality.⁽¹⁹⁾ That is why hyperuricemia is currently well-thought-out to be an important threat element for hypertension, metabolic syndrome and cardiovascular illness⁽²⁰⁾ including stroke and myocardial infarction. Excessive uric acid levels might forecast the risk for developing transient ischemic attack (TIA) and cardiac failure additionally being predictive of symptom status as well as prognosis.⁽²¹⁾ In this study, in hyperuricemia group, 48 were male and 42 female patients. This finding is consistent with Stelmech et al.⁽²²⁾ who confirmed in their research about advanced prevalence of hyperuricemia among male gender and a sturdier association of hyperuricemia with lipid profile in male young people. In this study total cholesterol, triglycerides, and LDL are directly proportional to upsurge in uric acid while HDL cholesterol is negatively connected with upsurges in uric acid. This outcome is similar to many researchers.^(9,18,23) The negative correlation of high density lipoprotein among patients

with raised uric acid ensued proliferation in atherosclerosis and in due course lead to ischemic heart disease. Plasma uric acid dimension might be worthwhile among the patients to recognize those at augmented threat for developing cardiovascular problems who might benefit from further triage and intervention. LDL is at all times considered to be bad cholesterol and upsurge in such cholesterol leads to worst consequences ranging from angina to myocardial infarction through developing atherosclerosis.⁽²³⁻²⁵⁾ Lippi concluded that identifying uric acid dimension timely might be supportive to detect the people who are at bigger risk of getting cardiovascular ailments.⁽²⁶⁾

CONCLUSION

This research work demonstrates that upsurges in uric acid levels are definitely related to dyslipidemia, and that may predispose such individuals to possible cardiovascular events. Consequently, preventive measures are required to identify such cases timely and manage properly to combat the risk of cardiovascular dysfunctions.

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EVALUATION OF RED BLOOD CELL INDICES IN PATIENTS OF FALCIPARUM MALARIA

Shahzad Ali Jiskani, Inayatullah Memon, Umair Ali Soomro, Shumail Siddiqui, Mehnaz Shaikh, Huma Abbasi

Department of Pathology, Indus Medical College Tando Muhammad Khan

Corresponding Author:

Shahzad Ali Jiskani,

MBBS, M. Phil (Haematology)
Senior Lecturer, Dept of Pathology,
Indus Medical College TMK

Co-Authors:

Inayatullah Memon

MBBS, MCPS (Clinical Pathology), M. Med,
Masters of Bioethics
Associate Professor, Department of
Pathology, Indus Medical College TMK

Umair Ali Soomro,

MBBS, M. Phil (Haematology)
Assist. Professor, Department of
Pathology, Indus Medical College TMK

Shumail Siddiqui

MBBS, M. Phil (Histopathology)
Assist. Professor, Department of
Pathology, Indus Medical College TMK

Mehnaz Shaikh, MBBS

Lecturer, Department of Pathology,
Indus Medical College TMK

Huma Abbasi, MBBS

Lecturer, Department of Pathology,
Indus Medical College TMK

Corresponding Author Email:

shahzadbaloach289@gmail.com

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88.76%, and 87.91%. Low values were found in MCV (57.91%), MCH (0%), and MCHC (0%). However, there was a important association between MCH and MCHC with malaria ($P < 0.01$).

ABSTRACT

OBJECTIVE: The aim of this study was to examine red cell indices seen at the Tertiary Care Hospital, in order to determine their usefulness in diagnosing falciparum malaria.

PATIENTS AND METHODS: This was a case control study. The study was performed from February 2018 to September 2018 at the Department of Pathology, Indus Medical College Tando Muhammad Khan. One hundred and ninety-six children aged 6 months to 40 years were recruited into the study including 98 diagnosed with malaria and 98 controls. The control subjects were recruited as no clinical features of malaria. Hematocrit (HCT), haemoglobin concentration (HB), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) were the following red cell indices obtained from the samples. The data was analysed using version 21.0 of SPSS. By measuring sensitivities, specificities, positive predictive and negative predictive values, the diagnostic precision was calculated. The accuracy of these statistics was tested using a confidence interval of 95%.

RESULTS: The HCT had a 80.04% sensitivity and an 82.15% specificity, while the HB had an 82.87 sensitivity and a 72.01 specificity. The positive predictive values for HCT and HB were respectively

CONCLUSION: The occurrence of anaemia would be a valuable supporting criterion in the diagnosis of malaria.

KEYWORDS: Malaria, Red cell indices, Diagnosis, Specificity, Sensitivity

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INTRODUCTION

Malaria has a major effect on global mortality rates; in 2015, it caused 429,000 deaths, with 70%, especially occurring in children under 5 years of age. It is also one of important cause of mortality and morbidity. Importing this is underlined by the fact that in 104 countries and territories malaria is regarded as endemic. The most lethal form and predominant form of extreme malaria is falciparum.⁽¹⁾

Malaria is preventable and treatable, but confirmation of diagnosis by microscopy or rapid diagnostic testing for each confirmed case is a key component of prevention and treatment measures.⁽¹⁻²⁾ These techniques are however limited and require some degree of practical ability. In semi-urban / resource-poor settings, these abilities are not always available. Therefore it is not unusual for clinicians to rely on clinical diagnostic methods.⁽³⁾ Plasmodium, an intra-erythrocytic parasite, is known to cause a wide variety of haematological changes.⁽⁴⁾ These changes can depend on factors like race, immunity levels, genes, nutritional status and socio-demographic conditions.⁽⁵⁾

This study aimed at evaluating the red cell indices of patients diagnosed with malaria at the Tertiary Care Hospital, with a view to determining their utility in aiding accurate diagnosis.

PATIENTS AND METHODS

This study was performed at the Department of Pathology, Indus Medical College Tando Muhammad Khan. This was a case control study. A total of 240 individuals aged 6 months to 40 years were recruited into the study, consisting of 120 diagnosed with malaria and 98 controls. The study was performed from February 2018 to September 2018. The ages and gender of all subjects have also been taken and registered. Study removed patients with evidence of other infectious diseases such as; typhoid fever, gastroenteritis, respiratory tract infections, acute bacterial meningitis or any other known cause of anaemia other than malaria.

Two millilitres (2 ml) of venous blood was drawn from all subjects into an EDTA anticoagulated

sample bottle and sent for examination to the laboratory. Blood in the sample bottles was also used to prepare thick and thin films to show Plasmodium falciparum and to conduct the rapid diagnostic test (RDT). Mindray BC-5000 haematology analyzer was used. The following red cell indices were obtained from the subjects; haematocrit (HCT), haemoglobin (HB), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH) and mean concentration of corpuscular haemoglobin (MCHC).

Confirmation of malaria diagnosis in the presence of any of the World Health Organization (WHO) case descriptions for serious malaria was provided with microscopy or rapid diagnostic tests (RDT).⁽²⁻⁶⁾ The thin and thick malaria parasite films were stained with Wright's stain and read by Microscopists. The RDT was performed using the Pf[®] rapid test kit for P. falciparum malaria. Effects on the control windows were recorded as positive or negative as shown by the coloured bands; test ('T') and control ('C') respectively. The same investigations were used in order to determine the absence of a significant malaria infection in the controls.

The data collected was entered in version 21.0. of the Social Science Statistical Package (SPSS) using the Chi-square test, categorical data was compared. The student t-test was used to make comparison between means. A p value less than 0.05 was considered to be statistically significant. By measuring the sensitivity, specificity, and predictive values, the diagnostic precision of the red blood cell indices was calculated.

RESULTS

Table 1 displays the bio data of the 240 study participants. malaria group's mean age was 23.25 ± 5.5 years, it varied non – significantly from the control group's mean age; 25.82 ± 6.17 years ($P = 0.09$). Males made up 61.25% (147) of the subjects under study, while females made up 93 subjects (38.75%). The mean red cell index of the malaria group and that of the controls are shown in Table 2. The mean

concentration of haematocrit, haemoglobin, the mean concentration of corpuscular haemoglobin and the mean concentration of corpuscular haemoglobin in the extreme malaria community varied significantly from that of the control group ($P < .001$). The mean MCV of the malaria group (81.18 ± 11.80 fL) did not, however, vary significantly from that of the control group (79.81 ± 8.91 fL), ($P = 0.41$). Table 2 also displays the sensitivity, accuracy,

and predictive values of all the measures. It indicates that there were strong sensitivities and specificities for HB and HCT, while MCV had 47.12% sensitivity and 44.91% percent specificity.

Table 3 compares the sex of the malaria group with their mean indices of red cells, and shows no statistically significant correlation between variables.

Table 1: General Characteristics in Each Group (n=240)

	Malaria Group (n=120)	Control Group (n=120)	t-value	p-value
Mean age (years)	23.25 \pm 5.5	25.82 \pm 6.17	2.82	0.09
Male/Female	76 (63.66%)/44 (36.66%)	71 (59.16%)/49 (40.83%)	-	0.17

Table 2: Red Cell Indices in Both Groups (n=240)

Mean Red cell Indices	Malaria Group (n=120)	Control Group (n=120)	t-value	p-value	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
HCT (%)	24.46 \pm 7.84	37.41 \pm 4.5	12.15	<0.001	80.04	82.15	88.76	72.37
Hb (g/dL)	6.94 \pm 2.95	11.48 \pm 2.05	8.98	<0.001	82.87	72.01	87.91	68.81
MCV (fL)	80.18 \pm 11.8	79.81 \pm 8.91	-0.78	0.41	47.12	44.91	57.91	37.87
MCH (pg)	21.23 \pm 2.98	24.78 \pm 3.61	-2.88	0.02	0	98.28	0	39.10
MCHC (g/dL)	33.67 \pm 2.87	30.89 \pm 2.97	-5.75	0.01	0	99.19	0	37.98

Table 3: Variables Between Gender Groups of Malaria Infected Patients (n=240)

Mean Red Cell Indices	Male (n=76)	Female (n=44)	P value
Hb (g/dL)	6.45 \pm 2.19	6.12 \pm 2.78	0.78
HCT (%)	21.13 \pm 7.87	20.01 \pm 7.41	0.69
MCV (fL)	82.19 \pm 8.45	81.10 \pm 10.03	0.75
MCH (pg)	24.18 \pm 3.01	23.98 \pm 2.98	0.87
MCHC (g/dL)	32.10 \pm 2.05	31.11 \pm 2.76	0.88

DISCUSSION

The present study clearly shows that anaemia (low HB) is prevalent in falciparum malaria and that a diagnosis of severe malaria (P value, high sensitivity, positive predictive and negative predictive values) may be indicated by its existence. This result is consistent with the generally held view of. ^(3-4, 7-10) However, the pathogenesis of anaemia in extreme malaria is not completely known; it is believed to derive from the interplay of many processes including: lysis of both parasitized and unparasitized erythrocytes, mopping up of parasitized erythrocytes by the RE system, dyserythropoiesis, parasite iron shunting, bone marrow suppression and red cell sequestration in deep capillaries. ⁽⁴⁾ Also noteworthy is the observed link between severe malarial anaemia, parasitic infections, dietary deficiencies of vitamins B₁₂ and E, folate and iron, and drug-related anaemia. ⁽⁹⁾ Our results do not suggest a utility in the diagnosis of malaria for MCV, MCH, and MCHC. However, higher values of MCH and MCHC among patients with malaria are relatively common enough to suggest that their existence should be recognised as possible warning signs (P values and specificities, respectively) This is similar to the outcomes of other studies. It is not known whether there is a correlation between red cell MCV, MCH as well as MCHC and malaria pathogenesis. ⁽⁴⁾ However, several studies have indicated that α / $\alpha\alpha$ thalassemia (microcytic states) selectively protects against malaria-associated anaemia, and that iron deficiency anaemia, a hypochromic microcytic condition also protects against the production of severe malaria in endemic areas. ⁽¹¹⁻¹³⁾

Furthermore, cross-sectional studies carried out in Cameroon showed a substantial increase in red cell indexes with a marked decrease in the prevalence of microcytic anaemia. This followed a decline in malaria prevalence that resulted from successful control measures. ⁽¹⁴⁾ These studies tend to give the impression that the relationship between these indices of red cells and malaria prevalence is positive. Nevertheless, our research's drawbacks, such

as a relatively small sample size may have limitations. Therefore, to establish the exact relation between these red cell indices and malaria in community, we suggest that larger, more detailed studies be performed. The findings in the present study agree with those of other studies that the impact of extreme malaria on haematological parameters has no gender preference. ^(4, 9)

CONCLUSION

As seen in patients of this area, we have shown the effects of malaria on certain haematological indices. HB and HCT were the most affected categories. We therefore suggest that the presence of anaemia in patients, in the presence of supporting clinical evidence, will be a valuable support criterion for the diagnosis of malaria. This will have a positive effect on prognosis as traditional management organisations will be introduced promptly.

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LETTER TO THE EDITOR: SHORT COURSE WITH LONG DURATION OF AZITHROMYCIN

Shahzad Ali Jiskani

Department of Pathology, Indus Medical College, Tando Muhammad Khan

Corresponding Author:

Shahzad Ali Jiskani

MBBS, M. Phil (Haematology)

Senior Lecturer, Department of Pathology
Indus Medical College Tando Muhammad
Khan

Corresponding author email:

shahzadbaloach289@gmail.com

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Royer and colleagues ⁽¹⁾ have performed a meta-analysis comparing shorter versus longer courses of antibiotics for treating infections in hospitalized patients. They concluded that shorter courses are safe. However, the authors do not address a flaw in the analysis; they included studies in which treatment with azithromycin was considered a short antibiotic course relative to treatment with another antibiotic. Azithromycin is a macrolide antibiotic

that has a relatively long terminal serum half-life, which has been reported to be 35-96 hours. ⁽²⁻⁴⁾ Moreover, the half-life of azithromycin in lung tissue can be as long as 132 hours, ⁽⁴⁾ which is important because tissue concentrations are thought to be more indicative of the clinical efficacy of macrolides. ⁽⁵⁾ In 4 of 19 studies in the meta-analysis, ⁽¹⁾ azithromycin was used as a short course for the treatment of pneumonia and compared with longer courses of antibiotics with a much shorter half-life. This implies that in these studies, the duration of the effective antibiotic tissue concentration in the short arms was probably not shorter than in the comparator arms. It could even be longer due to azithromycin's favourable pharmacokinetics. In my view, these studies have unfairly contributed to the clinical efficacy of short courses, thereby threatening the validity of the overall conclusions. I think that effective antibiotic blood/tissue levels determine the clinical outcome, not just shorter or longer antibiotic courses.

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Hyderabad Road, Tando Muhammad Khan, Sindh Pakistan
Phones: +92-22-3409562, 67 & +92-333-2711606, Fax: +92-22-3409559
Web: www.jimc.org.pk, Email: info@jimc.org.pk