Pakistan Journal of Neurological Sciences (PJNS)

Volume 19 | Issue 1 Article 9

3-2024

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https://doi.org/10.56310/pjns.v19i01.303

BEYOND THE MOSQUITO STING: GUILLAIN-BARRE SYNDROME FOLLOWING MALARIAL SEASONAL SURGE

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Date of submission: *October 17, 2023* ***Date of revision:*** *March 11, 2024* ***Date of acceptance:*** *March 22, 2024*

ABSTRACT

Background and objective:
Malaria, a prevalent disease most commonly caused by Plasmodium vivax and falciparum, frequently leads to intricate neurological complications. The objective of this study was to study Guillain-Barre syndrome as a prevalent neurological manifestation of malaria.

Methods:
A cross-sectional observational study was undertaken at Neurology Department of Chandka Medical College Hospital in Larkana, from April 2023 to September 2023 during the seasonal peak of malaria. The study included 20 patients who met the specified criteria. SPSS version 23.0 was used for data analysis.

Results:
Among the 20 patients who developed Guillain-Barre Syndrome following malaria infection, 18 exhibited axonal degeneration, while three had the demyelinating variety. The majority of cases presented with a combination of sensory and motor nerve involvement. Encouragingly, the prognosis was favorable, with a 70% recovery rate.

Conclusion:
Our study highlights a significant association between Guillain-Barré Syndrome and post-malaria complications, with a overall positive prognosis.

Key words:
Guillain-Barre syndrome, Malaria, Plasmodium vivax, Plasmodium falciparum, Acute inflammatory demyelinating polyneuropathy , Demyelinating disorders, Axonal disorders

INTRODUCTION

Guillain-Barre syndrome is an acute or subacute onset monophasic demyelinating disorder impacting the peripheral nerves. Acute inflammatory demyelinating polyradiculoneuropathy is an infrequent outcome following parasitic infections, with its typical occurrences associated with post bacterial, viral infections, or immunization.[1] GBS usually manifests subsequent to viral upper respiratory tract or gastrointestinal infections, with Campylobacter jejuni being a prevalent culprit. Other infections like HIV, Zika virus, cytomegalovirus, Epstein-Barr virus, hepatitis viruses, SARS-19, Hemophilus influenzae, Brucella, Mycoplasma, Yersenia, Toxoplasmosis, Parainfluenza, Influenza virus, Coxsackie, Vaccinia, Herpes simplex, West Nile virus and Escherichia coli have also been linked to GBS. Notably, Plasmodium vivax malaria triggering GBS is exceedingly uncommon, documented sparsely in literature.[2] P. falciparum and vivax both infections are recognized for their potential neurological aftermath. Malaria exhibits diverse neurological manifestations, encompassing cerebral malaria, post-malarialneurological syndrome (PMNS), polyneuritis, psychosis,posterior reversible encephalopathy syndrome (PRES), acute febrile encephalopathy, reversible cerebral vasoconstriction syndrome (RCVS), Guillain-Barre syndrome (GBS), malarial retinopathy, acute disseminated encephalomyelitis (ADEM), and cerebellar ataxia.[3]

Among those living in malaria-prone areas or individuals returning from regions endemic to malaria, who present symptoms of acute inflay demyelinating

polyradiculoneuropathy amid an ongoing fever or a recent febrile episode, malarial infection warrants consideration as a potential triggering factor.[4] Other Protozoas like Leishmania donovani, alongside Plasmodium vivax and falciparum, have been outlined in case reports, albeit in a limited number of patients showing an association.[5] The precise mechanism of this peripheral nerve disease following plasmodium infection remains elusive. Potential mechanisms for this phenomenon may involve the altered shape of parasitized red blood cells causing obstruction within the vasa nervorum, along with release of neurotoxins leading to metabolic, physiological, nutritional and biochemical disturbances.[6,7]

Within Pakistan, the pooled malaria prevalence among infections amounts to 23.3%, with vivax, falciparum, and other combined infections comprising 79.13%, 16.29%, and 3.98%, respectively.[8] Notably, the incidence of GBS displays seasonal variation, often attributed to the heightened activity of the underlying offending agent. In light of the aforementioned observations, associating GBS with malarial infections, particularly the rare link to Plasmodium vivax, there emerges a crucial query: Could a deeper exploration of this connection unveil vital insights into the intricate interplay between parasitic infections and peripheral nerve disorders? Also, given the seasonal patterns of GBS linked to malaria in places like Pakistan, should healthcare professionals in these areas be more watchful for GBS after malarial infections? These queries emphasize the need for further investigation and awareness to enhance our understanding of this intriguing medical nexus.

In the region of Larkana, Sindh, the months from April to September experience a notable rise in malaria cases, attributed to favorable environmental conditions for the breeding of the mosquito vector during the prior rainy season in April and May. At the conclusion of September 2023, a surge in GBS cases among hospital admissions prompted an investigation into the potential correlation between this disease and malaria.

METHODS

This prospective cross-sectional observational study was performed at Neurology Department of Chandka Medical College Hospital in Larkana, one of the few hospitals in the interior Sindh offering specialized neurology services, from April 2023 to September 2023. This study included a total of 20 patients. Patients were enrolled via non-probability consecutive sampling. The Study was approved by ethical review committee of Shaheed Mohtarma Benazir Bhutto Medical University Larkana ethical committee.

Inclusion criteria: All the patients with age greater than 18 years, positive MP test, visualization of parasite on smear, fulfilling Asbury diagnostic criteria for GBS, supported by nerve conduction studies (NCS).

Exclusion criteria: All the patients with age less than 18, recent vaccination, pre-existing neurological conditions were excluded from study.

Data collection: All patients with the diagnosis of GBS post-malaria were enrolled in this study. Data collection encompassed age, gender, medical history, physical examinations, antimalarial drug treatments, and blood film analysis to identify malaria parasites and their species. NCS was conducted using a Neurowerk machine. Serologic testing for various pathogens and routine laboratory tests were performed to rule out alternative causes for polyneuropathy. Patients were monitored post-discharge at the outpatient neurology clinic.

Statistical analysis: The Data collection, tabulation and analysis was performed through SPSS version 23.0.

RESULTS

Twelve men (80%) and eight women (60%), mostly from the rural areas with middle socioeconomic background class, presented with GBS following malaria. Their ages ranged between 18 and 60 years (mean, 34.5 ±16.5 years).The patients had fever for three to thirty days (mean, 11.6 ±7.9 days) preceding the onset of polyneuropathy.

Sixteen patients exhibited antecedent rigors and chills, three manifested cough symptoms, and one presented with antecedent diarrhea and vomiting concomitant with fever. No obvious cause other than malaria was found to explain the fever including the four patients with preceding respiratory and gastrointestinal complains.

Blood smears confirmed the presence of P. vivax in 14 patients and P. falciparum malaria in six patients. Blood serology, cell counts, blood chemistry and urine analysis findings were within normal limits. For

treatment of malaria, initially all of the patients received combined sulfadoxine-pyrimethamine tablets (Fansidar); six were found to have resistant infection and they received Artemether-Lumefantrine tablets twice daily for three more days after the initial course.

All the patients developed a rapidly progressive limb weakness that reached its nadir within two weeks (mean, 8.9 ±4.6 days). Figure 1 illustrates the type of neuropathy detected in the population.

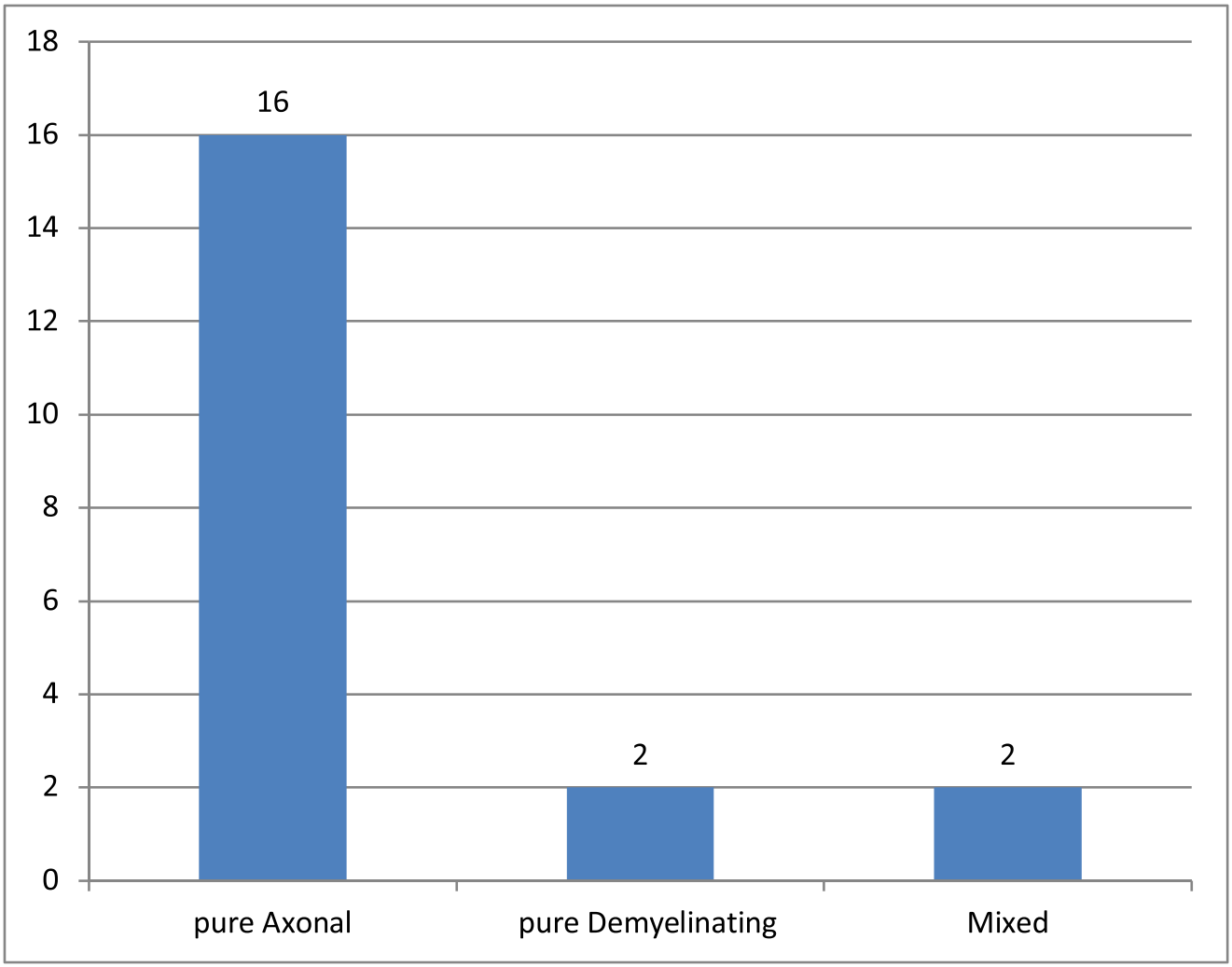

Figure 1: Type of neuropathy detected in the patients

Seventeen patients demonstrated sensorimotor nerve involvement, while three patients exhibited solely motor neuropathy. Outcome was that 11 patients recovered with good motor power having GBS Hughes Disability Scale grade 1, six patients reached grade 2 but continued to show persistent generalized areflexia. No patient remained in grades 3 to 5, while three patients with bulbar and respiratory paralysis died of cardiopulmonary complications (grade 6).

Table 1 summarizes the characteristics of all the 20 patients.

Table 1: Summary of the study population

Sr. No	Age	Gender	PRECEDING SYMPTOMS	Fever duration before GBS, d	Peak Muscle paralysis, d	MP / MP ICT	PLASMODIUM SPECIES	NCS DM	NCS AXONAL	TYPE OF NEUROPATHY	ANTIMALIRIAL THERAPY	IMMUNO MODULATORY THERAPY	OUT COME
1	22Y	FEMALE	rigors and chills	5	10	yes	falciparum	**NO**	YES	SM	YES	PLASMA	D
2	42Y	MALE	rigors and chills	6	10	YES	Vivax	NO	yes	SM	YES	NO	R
3	42Y	FEMALE	rigors and chills	8	14	yes	Vivax	NO	YES	SM	YES	NO	R
4	41Y	MALE	rigors and chills	5	12	YES	Vivax	NO	YES	SM	YES	NO	R
5	21Y	FEMALE	rigors and chills	6	14	yes	vivax	YES	NO	SM	YES	PLASMA	D
6	20Y	FEMALE	rigors and chills	4	10	yes	falciparum	NO	YES	SM	YES	NO	R
7	38Y	FEMALE	rigors and chills	5	11	YES	falciparum	NO	YES	SM	YES	NO	R
8	20Y	FEMALE	rigors and chills	9	21	YES	Vivax	YES	YES	SM	YES	PLASMA	R
9	12Y	MALE	respiratory illness	5	10	yes	Vivax	NO	YES	SM	YES	NO	R
10	28Y	MALE	rigors and chills	8	14	yes	falciparum	NO	YES	SM	YES	NO	R
11	45Y	FEMALE	rigors and chills	10	20	yes	falciparum	NO	YES	SM	YES	PLASMA	R
12	30Y	FEMALE	rigors and chills	8	18	yes	Vivax	YES	NO	SM	YES	NO	R
13	38Y	MALE	respiratory illness	8	16	yes	Vivax	NO	YES	M	YES	PLASMA	D
14	25Y	MALE	Respiratory illness	6	14	yes	Vivax	NO	YES	SM	YES	NO	R
15	25Y	MALE	rigors and chills	5	10	yes	falciparum	NO	YES	M	YES	NO	R
16	35Y	FEMALE	rigors and chills	7	14	yes	Vivax	NO	YES	SM	YES	NO	R
17	40Y	MALE	rigors and chills	8	20	YES	Vivax	NO	YES	SM	YES	NO	R
18	35	MALE	GIT illness	5	19	YES	Vivax	NO	YES	M	YES	NO	R
19	51Y	MALE	rigors and chills	8	21	YES	Vivax	NO	YES	SM	YES	PLASMA	R
20	23 WV +D	FEMALE	rigors and chills	5	18	yes	V"}VivaxJ'4	YES	YES	SM	YES	NO	R

d=days, DM=demyelinating, SM=sensory-motor, M=motor, D=deteriorated, R=recovered

DISCUSSION

GBS is characterized by immuno-mediated damage to peripheral nerves, typically triggered by infections or vaccinations. More than two-thirds of cases have preceding gastrointestinal or respiratory infections. Various infectious agents, primarily viruses, have been implicated, with limited reports of protozoal parasitic infections such as L. donovani, P. falciparum, and P. vivax malaria.[9] Recent research delineates GBS into distinct variants with differing clinical, etiologic, and pathologic features. Major acute paralytic variants include AIDP, primarily demyelinating, and few axonal degeneration forms, like acute sensory motor axonal neuropathy (AMSAN) and acute motor axonal neuropathy (AMAN).[10]

Molecular mimicry, epitopes shared by the microorganism and peripheral nerves, is believed to underlie the immune-mediated attack causing myelin and axonal damage. Neurophysiologic studie opatients revealed predominantly axonal degeneration in both motor and sensory nerves and a few having demyelinating features, consistent with AIDP.[11] The observed seasonal rise in GBS incidence during and after the rainy season aligns with the flare-up of the

offending agent, often associated with vector mosquito breeding and increased malaria morbidity in Larkana. This epidemic of GBS may be attributed to a mutant strain of Plasmodium species with novel surface antigen properties, considering the ability of malaria parasites to exhibit antigenic variation altering host immune responses.[12] The mortality rate in our patients was 20% primarily due to cardiopulmonary complications during severe respiratory paralysis necessitating mechanical ventilation. The heightened incidence of bulbar involvement likely contributes to this mortality rate.[13]

CONCLUSION

There was a significant association between Guillain-Barre Syndrome and malaria, with an overall positive prognosis with a 70% recovery rate. These insights contribute to our understanding of the neurological manifestations of malaria and provide valuable information for clinical management and future research. Further comprehensive large scale epidemiologic and immunopathologic studies are imperative to establish the association and elucidate the mechanisms of GBS in malaria.

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Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil

Author's contribution:
Sana Ghous; data collection, data analysis, manuscript writing, manuscript review
Alam Ibrahim Siddiqui; concept, data collection, data analysis, manuscript writing, manuscript review
Abdul Rahman Soomro; data collection, data analysis, manuscript writing, manuscript review
Abu Bakar Shaikh; concept, data collection, manuscript writing
Sajjad Hussain Jalbani; concept, data collection, manuscript writing
Abdul Ghafoor Magsi; concept, manuscript revision

The authors have approved the final version of the article, and agree to be accountable for all aspects of the work.