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Review Article

Mustard oil consumption and Harris platelet syndrome: unveiling a dietary link to thrombocytopenia in the Indian subcontinent

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Abstract

Background and objectives: Asymptomatic thrombocytopenia, characterized by a reduced platelet count without bleeding symptoms, is notably prevalent in certain regions of India and Bangladesh, presenting a diagnostic challenge. A significant portion of healthy blood donors from Bangladesh and various parts of India, particularly West Bengal, exhibit this condition, termed Harris platelet syndrome (HPS). This review explores the potential correlation between mustard oil consumption, a common dietary staple in these regions, and the incidence of HPS.

Methods: A comprehensive narrative review was conducted using systematic search strategies across databases such as Google Scholar, MEDLINE, PubMed, and Scopus. Keywords included "Harris platelet syndrome," "mustard oil consumption," "thrombocytopenia," and "erucic acid." Studies were selected based on relevance and quality, focusing on the epidemiology of HPS, dietary habits, and the thrombocytopenic effects of erucic acid.

Results: HPS shows a significant geographical prevalence in the Indian subcontinent, notably in regions like West Bengal, Kashmir, and Assam. The review identifies a higher prevalence of thrombocytopenia in areas with predominant mustard oil usage. Studies highlight the association between dietary erucic acid from mustard oil and thrombocytopenia, with notable effects observed in patients treated with Lorenzo's Oil, which contains erucic acid.

Conclusions: The review highlights a significant association between mustard oil consumption and asymptomatic thrombocytopenia in the Indian subcontinent. The similarity in hematological profiles between HPS and erucic acid-induced thrombocytopenia underscores the need for further research. This includes measuring erucic acid levels in patients, conducting controlled dietary interventions, and genetic analyses to differentiate between genetic and environmental factors.

Introduction

Asymptomatic thrombocytopenia, characterized by a reduced platelet count without bleeding symptoms, is prevalent in certain regions of India and Bangladesh. This poses a diagnostic challenge for clinicians encountering patients with unexplained low platelet counts during routine checkups. Although comprehensive epidemiological data for Bangladesh are sparse, a pivotal study conducted at Christian Medical College revealed

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that 8.5% of healthy blood donors from Bangladesh exhibited asymptomatic thrombocytopenia, which was arbitrarily diagnosed as Harris platelet syndrome (HPS) [1].

HPS, originally termed asymptomatic constitutional macrothrombocytopaenia (ACMT), was first identified in blood donors from West Bengal [2]. It was later renamed Harris platelet syndrome (HPS) to avoid confusion with congenital amegakaryocytic thrombocytopenia [1]. HPS is defined by the presence of thrombocytopenia and giant platelets without bleeding symptoms or MYH9 mutations. The disorder appears to be inherited in an autosomal dominant manner, although the specific genes responsible for HPS remain unidentified [1].

The geographic prevalence of HPS in the Indian subcontinent, particularly in regions such as West Bengal, Kashmir, and Assam, suggests a regional pattern influenced by genetic and environmental factors. One intriguing hypothesis is the potential link between dietary habits, specifically mustard oil consumption, and the prevalence of thrombocytopenia [3]. Mustard oil, rich in erucic acid, is a staple in many parts of Northern and Eastern India and neighbouring countries [4]. The potential thrombocytopenic effects of erucic acid, evidenced in conditions like adrenoleukodystrophy (ALD) treated with Lorenzo's Oil, further underscore the need to investigate this association [5-7].

This review aims to explore the epidemiology of HPS in the Indian subcontinent, its potential correlation with mustard oil consumption, and the underlying pathophysiology of erucic acid-induced thrombocytopenia.

Materials and methods

This narrative review synthesizes insights from a comprehensive examination of scientific journals and authoritative sources, focusing on the epidemiology of HPS in the Indian subcontinent, its associations with mustard oil consumption, and the underlying pathophysiology of mustard oil-induced thrombocytopenia.

To gather relevant data, a systematic search strategy was employed using keywords such as "constitutional asymptomatic macrothrombocytopenia," "Harris platelet syndrome," "mustard oil consumption," "epidemiology," "Indian subcontinent," and "erucic acid." Various databases, including Google Scholar, MEDLINE, PubMed, and Scopus, were utilized, with no restrictions on the search scope.

Exclusion criteria were applied to non-English articles. Researcher independently conducted article searches and evaluated the quality of each study. The inclusion of studies in the review was based on a thorough examination of the full text, ensuring the relevance and reliability of the data presented.

Results

Regional prevalence and characteristics

HPS exhibits a distinct geographic distribution, with significant prevalence in the Indian subcontinent, particularly in northern and eastern regions such as Kashmir, West Bengal, and Assam, with potential extensions to Bangladesh, Nepal, and Bhutan (Figure-1, Table-1). A study at Christian Medical College, Vellore, screened 10,200 blood donors and found that prevalence rates are highest in Eastern India (35%), followed by Northern India (18%), Western India (8.5%), Southern India (4.5%), and neighbouring countries (8.5%) [1].

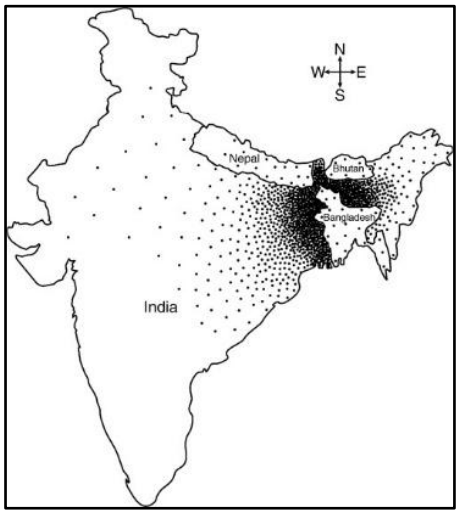

Figure-1: *The geographic distribution of HPS. The dotted area indicates distribution of HPS cases [1].*

Summary of studies on macrothrombocytopenia in different regions of India is presented in Table-2.

Table-1: *Geographical distribution of Harris platelet syndrome [1]*

Region	Donors Number	Cases having thrombocytopenia n (%)	Normal platelet count n (%)	Mean platelet volume (fL; mean ± SD)	Mean platelet count ($\times 10^9$/L; mean ± SD)
Eastern India	390	136 (35)	254 (65)	10.7 ± 2.1	213 ± 59
Northern India	132	24 (18)	108 (82)	9.3 ± 2.2	213 ± 81
Western India	141	12 (8.5)	129 (91.5)	8 ± 1.6	263 ± 81
Southern India	268	12 (4.5)	256 (95.5)	7.6 ± 1.1	250 ± 66
Neighbouring Countries	71	6 (8.5)	65 (91.5)	9.2 ± 2	211 ± 68

Table-2: *Summary of studies on macrothrombocytopenia in different regions of India*

Author/Year of publication	Study region and population	Key Findings
Edupuganti *et al*. [8], 2020	South India. 300 north and north-eastern immigrants (cases) and equal number of healthy subjects from south India (controls)	Significant prevalence of macrothrombocytopenia among immigrants from north-eastern region of India (4.3% of cases *vs*. 0.66% of controls).
Bhola *et al*. [9], 2023	Himachal Pradesh. Patients in a hospital setting	MPD was significantly higher (3.5 ± 1.1µm) in patients with likely inherited macrothrombocytopenia compared to those with secondary thrombocytopenia (2.4 ± 0.7µm) and control group (1.9 ± 0.7µm).
Ali *et al*. [10], 2016	India. Total 112 cases	Candidate gene defects were identified in 48 cases. There were 23 gene defects, majority missense variations in GP9, ABCG5, GP1BB, GP1BA, MYH9; highlights genetic heterogeneity
Naina *et al*. [11], 2010	North-eastern India. RBC and platelet indices of blood donors with HPS from the north-eastern part of India compared with blood indices of blood donors of south India	Lower platelet count, higher MPV in donors with HPS; significant differences in platelet biomass and RDW compared to donors from south India. Peripheral blood smears showed giant platelets and thrombocytopenia in HPS donors, with no abnormal RBC morphology
Naina *et al*. [12], 2002	West Bengal. Healthy blood donors: 76 from Tamil Nadu (south India) and 78 from West Bengal (northeast India)	32.4% West Bengal donors had thrombocytopenia and 64 (82.1%) had giant platelets (MPV >10 fL; range 7.5-16.8 fL). All donors exhibited normal RBC morphology with no leukocyte inclusion bodies or history of excessive bleeding. Platelet function tests were normal. Family studies suggested possible genetic inheritance, and the condition was described as ACMT
Kakkar *et al*. [13], 2015	North India. Patients in a hospital setting.	CBC evaluation revealed macrothrombocytopenia in 75 (0.6 %) patients, majority (96 %) of North Indian origin. Higher MPV in patients with macrothrombocytopenia; significant difference in MPV compared to those with secondary thrombocytopenia and ITP.

Patel et *al*. [14], 2019	Western India. 10,047 healthy college students from the city of Surat (western India) were investigated for macrothrombocytopenia	Only 1.95% of the healthy population had macrothrombocytopenia. Asymptomatic macrothrombocytopenia is rare in western parts of India
Ali *et al*. [15], 2015	North-eastern India. Five subjects with BMTCP, platelet counts ranging from 36 to 140 × 10^9/L, and MPV between 13.5 - 16.1 fL, were analysed for differential gene expression using suppressive subtractive hybridization (SSH).	Identified differential gene expression in MTMR9, IREB2, TUBA, TKL; highlights multifactorial aetiology of BMTCP
Lorenzo *et al*. [16], 2014	Kashmir Valley. The study included 830 healthy male blood donors from the Kashmir Valley.	Fifteen percent donors had thrombocytopenia; mean platelet count - 109.6 x 10^9/L compared to 189.9 x 10^9/L in controls ($p < 0.0001$). High prevalence of IGPD with mild to severe thrombocytopenia; higher MPV and RDW in affected individuals; no associated bleeding symptoms
Sultan *et al*. [17], 2019	Upper Assam. Study population: 510 healthy volunteers consisting of 46% males and 54% females	25.3% (n = 129) had low platelet count. Mean MPV was significantly higher in low platelet count group as compared to the normal group ($p < 0.001$). Age, gender, ethnicity, and MPV are significantly associated with platelet count variation. Heterozygosity of the risk allele does not contribute to the low platelet count condition.

Note: RBC - red blood cells, RDW - red cell distribution width, MPV – mean platelet volume, MPD - mean platelet diameter, ACMT- asymptomatic constitutional macrothrombocytopenia, BMTCP - *Bengal macrothrombocytopenia, IGPD – inherited giant platelet disorders.*

Key findings indicate significant regional variations in the prevalence of *macrothrombocytopenia*, with higher rates among people of north and eastern regions compared to other areas. Diagnostic advancements, such as the use of automated complete blood count (CBC) data and platelet histograms have been proven effective in identifying this condition. Genetic studies highlight the heterogeneity of macrothrombocytopenia. Clinical characteristics often include lower platelet counts and increased mean platelet volume, with no significant bleeding symptoms in most cases.

Thrombocytopenia and mustard oil consumption

The geographical distribution of HPS closely aligns with regions in the Indian subcontinent where mustard oil is commonly used as the primary cooking oil [1,4]. In contrast, regions where mustard oil is less popular, such as the southern and western parts of India, exhibit lower instances of thrombocytopenia.

A study conducted in southern India highlights this disparity, revealing a significant difference in the prevalence of thrombocytopenia between immigrants from northern and north-eastern India (4.3%) and the local southern Indian population (0.66%) [8]. Similarly, asymptomatic thrombocytopenia is relatively uncommon in western India, with a study in Surat reporting its prevalence of only 1.95% among healthy college students [14]. These observations suggest a potential correlation between dietary habits, specifically mustard oil consumption, and thrombocytopenia prevalence. A case-control study in the Bangladeshi population found a significant link between mustard oil use and thrombocytopenia, with 83.3% of thrombocytopenia cases reporting mustard oil consumption compared to 28.3% of controls [3].

Erucic acid: the main contributor to mustard oil-associated thrombocytopenia

Mustard oil, commonly used in Eastern and Northern India, contains high levels of erucic acid. Commercial varieties have 41.8% erucic acid, while traditional Ghani mustard oil contains about 51.98% [18]. Erucic acid, a monounsaturated omega-9 fatty acid also found in rapeseed oil, has been linked to thrombocytopenia in animal studies and in patients treated with Lorenzo's oil, a therapeutic agent containing 20% erucic acid [5-7,19]. Several studies

Table-3: *Key Findings of the studies on the haematological effects of Lorenzo's Oil/erucic acid in ALD patients*

Author/Year of publication	Study population	Key Findings
Aubourg *et al*. [22]	Twenty four patients with AMN	Six patients developed asymptomatic thrombocytopenia (platelet count < 100,000 cells/mm³). No significant changes in other haematological parameters or platelet function tests.
Zinkham *et al*. [6]	Forty six patients with ALD	Significant platelet count decreased in 19 patients (41%). Platelet size increased in patients with thrombocytopenia, showing an inverse correlation with platelet count. Platelet levels of erucic acid markedly elevated in patients with thrombocytopenia. Platelet count returned to normal within 2 - 3 months after stopping erucic acid. Minor bruising occurred in some patients, but no major bleeding events.
Konijnenberg *et al*. [23]	Seventeen adult X-linked ALD patients	Thrombocytopenia observed in 7 very compliant patients. Mean platelet volume increased. Enhanced *in-vivo* platelet activation indicated by increased surface expression of P-selectin (CD62P) and fibrinogen receptor (PAC-1) in affected patients.
van Geel *et al*. [24]	Twenty two X-linked ALD patients treated with Lorenzo's oil	Mild increase in liver enzymes in 55% patients, thrombocytopenia (in 55% patients), mild decreases in haemoglobin concentration and leukocyte count. Platelet counts significantly decreased.
Chai *et al*. [25]	Case report of a patient using Lorenzo's oil	A 37-year-old man with AMN experienced a significant drop in platelet count from 242 x 10^3/µL to 133 x 10^3/µL within four weeks after starting Lorenzo's oil. Upon discontinuing Lorenzo's oil and reverting to glycerol trioleate, platelet count normalized within one week and returned to pre-treatment levels within three weeks.
Zierz et al.[5], 1993	Five X-ALD patients	Thrombocytopenia in all patients, with platelet counts ranging from 37,000 to 84,000/mm³. Mean platelet volumes abnormally increased. Thrombocytopenia was fully reversible after discontinuation of glycerol trioleate and glycerol trierucate (GTE). Bone marrow biopsies showed no evidence of reduced megakaryocytopoiesis.
Shin *et al*. [21], 2015	Case report of a AMN patient	Romiplostim effectively mitigated the thrombocytopenia caused by mustard oil.
Crowther *et al*. [26], 1995	Case report of a ALD patient treated with erucic acid	Profound thrombocytopenia observed.

Note: ALD - adrenoleukodystrophy, AMN - adrenomyeloneuropathy.

have explored the impact of erucic acid on platelet count and morphology. A study on 46 ALD patients treated with Lorenzo's Oil observed significant thrombocytopenia in 19 patients, with platelet counts inversely correlated with erucic acid levels and platelet size. Thrombocytopenia resolved within 2 to 3 months after discontinuing erucic acid [6]. Another study reported decreased platelet counts in five patients with X-linked ALD upon erucic acid administration, with marked thrombocytopenia in three patients. Thrombocytopenia was fully reversible after discontinuing erucic acid [5]. A study by Johns Hopkins University found a significant decrease in mean platelet count over six months in ALD patients treated with Lorenzo's Oil, with alterations in platelet size and structure but no consistent abnormalities in platelet function tests [7].

Historical data also support the thrombocytopenic effects of erucic acid, as seen with rapeseed oil [20]. Additionally, a case report of a 73-year-old man with ALD who developed thrombocytopenia after using mustard oil further supports this association [21]. Key findings of the studies on the haematological effects of erucic acid in ALD patients are summarize in Table-3.

Discussion

The findings from this review highlight a significant geographical overlap between the prevalence of HPS and regions with high mustard oil consumption. The shared hematological profile between HPS and erucic acid-related thrombocytopenia, including thrombocytopenia with giant platelets and normal platelet function tests, suggests potential common underlying mechanisms. Despite significant reductions in platelet counts, the absence of bleeding symptoms indicates intact platelet functionality, a crucial clinical observation.

The stable, non-progressive nature of HPS and the reversibility of erucic acid-related thrombocytopenia upon discontinuation of erucic acid intake highlight the potential influence of environmental factors, particularly dietary habits, in its aetiology. The exclusion of MYH9 mutations and other systemic issues reinforces the hypothesis of a dietary link with the condition.

Given the high prevalence of mustard oil use in regions with notable HPS cases, dietary erucic acid could be a significant environmental contributor to thrombocytopenia. This correlation calls for more focused research to distinguish between the genetic basis of HPS and the environmental impacts of mustard oil consumption. Studies involving direct measurement of erucic acid levels in patients with HPS, alongside controlled dietary interventions and genetic analyses, are essential to elucidate the precise relationship between mustard oil and thrombocytopenia. Further research should explore the potential health implications for populations with high dietary intake of erucic acid. Understanding these correlations could lead to better management and prevention strategies for thrombocytopenia cases in affected regions.

In conclusion, this review highlights the significant association between mustard oil consumption and asymptomatic thrombocytopenia in the Indian subcontinent. By drawing attention to the similarities between HPS and erucic acid-related thrombocytopenia, it provides a compelling case for further investigation into dietary influences on platelet biology. Enhanced understanding of these relationships could lead to improved diagnostic, therapeutic, and preventive strategies, ultimately benefiting the population at risk.

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