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Haematological and Biochemical Changes During Adjunctive Biobran (MGN-3) Treatment in Patients with Haematological Malignancies: A Prospective Observational Study

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Abstract

Background: Biobran (MGN-3), a rice bran-derived arabinoxylan compound, has demonstrated immunomodulatory properties. However, evidence regarding its haematological effects and safety in patients with haematological malignancies remains limited. This study evaluated haematological changes and clinical tolerability during adjunctive Biobran administration.

Methods: This prospective, single-center, single-arm study was conducted at Green Life Hospital, Dhaka, Bangladesh. A total of 22 newly diagnosed patients with haematological malignancies were enrolled between May and December 2024 and followed up through June 2026. All patients received oral Biobran (MGN-3) at 1 g/day alongside conventional anticancer treatment. Haematological parameters were assessed across five visits, while liver and kidney function were evaluated across four visits. Cytopenias, adverse events, supportive medication use, and hospitalisation were also recorded.

Results: Mean haemoglobin increased from 9.7 ± 1.6 to 11.2 ± 0.7 g/dL, and RBC count increased from 3.41 ± 0.63 to 3.84 ± 0.38 × 10^{12}/L (both $p < 0.001$). Anaemia prevalence decreased from 54.5% to 4.5%. Neutrophil, lymphocyte, and platelet counts fluctuated significantly across visits (all $p < 0.001$), without significant baseline-to-final differences. Serum albumin increased ($p < 0.001$), while creatinine decreased ($p = 0.024$) and eGFR increased ($p = 0.032$). Modest increases in bilirubin and AST were observed. Nausea or vomiting (72.7%), anorexia (68.2%), and weight loss (63.6%) were frequently reported. Antibiotic or antifungal use occurred in 31.8%, and hospitalisation in 18.2%.

Conclusion: Haematological improvement and modest changes in liver and kidney function were observed during adjunctive Biobran administration. However, its independent efficacy and safety could not be established because of the small sample size, heterogeneous treatments, and absence of a control group. Larger controlled studies are warranted.

Keywords: Biobran, MGN-3, Haematological Malignancies, Haematological Parameters, Cytopenia, Adjunctive Therapy

1. Introduction

Haematological malignancies comprise a diverse group of disorders, including leukaemia, lymphoma, and multiple myeloma, which arise from abnormal proliferation of blood-forming and lymphoid cells. Despite advances in chemotherapy, targeted therapy, and immunotherapy, their management remains challenging. Both the underlying disease and anticancer treatment may cause bone marrow suppression, cytopenias, impaired immune function, and treatment-related complications. These conditions may increase the risk of infection, require supportive care, and affect patients' tolerance of treatment [1-3].

Supportive care plays an important role in the management of haematological malignancies, particularly among patients receiving intensive chemotherapy. Cancer-associated anaemia and treatment-related cytopenias may contribute to fatigue, infection, bleeding complications, and treatment interruptions [1, 4, 5]. Various nutritional and immunomodulatory agents have been investigated for their potential supportive role during anticancer treatment. Among these, Biobran (MGN-3), a modified arabinoxylan compound derived from rice bran, has attracted interest because of its reported immunomodulatory properties [6, 7].

Experimental investigations have demonstrated that Biobran may influence several components of the immune system, particularly natural killer (NK) cells, dendritic cells, and other immune responses [8-11]. Clinical studies have also reported changes in selected immune parameters following Biobran supplementation. In a randomized placebo-controlled study involving patients with multiple myeloma, Cholujova *et al*. [12] reported increased NK cell activity and changes in dendritic cell populations and selected cytokines. Similarly, Elsaid *et al*. [13] observed enhanced NK cell activity among older adults receiving Biobran supplementation. Other clinical investigations have explored its effects on immune responses and health-related quality of life in older adults [14, 15].

The potential role of Biobran as an adjunct to conventional cancer treatment has also been investigated. A randomized clinical trial involving patients with hepatocellular carcinoma reported favourable treatment-related outcomes following adjunctive MGN-3 administration [16]. More recently, clinical investigations have explored the effects of rice bran arabinoxylan compound on quality of life among patients receiving active cancer treatment [17, 18]. However, these findings cannot be directly generalised to patients with haematological malignancies because of differences in study populations, treatment regimens, and outcome measures.

Although these investigations suggest potential immunomodulatory and supportive effects, evidence regarding the clinical benefits of Biobran remains limited. Most available studies have involved relatively small populations, and several have primarily assessed immunological or patient-reported outcomes rather than routine haematological parameters [6, 7]. Furthermore, information regarding changes in blood counts, liver and kidney function, and treatment tolerability among patients with different haematological malignancies is limited.

Therefore, the present study aimed to evaluate changes in haematological parameters among patients with haematological malignancies receiving Biobran (MGN-3) alongside conventional anticancer treatment. Changes in liver and kidney function, the frequency of cytopenias, and reported adverse events were also assessed to describe the laboratory safety profile and clinical tolerability during treatment.

2. Materials and Methods

2.1 Study Design and Setting

This prospective, single-centre, single-arm study was conducted at Green Life Hospital, Dhaka, Bangladesh. Patients were enrolled between May and December 2024, and follow-up assessments were conducted from January 2025 to June 2026. The study aimed to evaluate changes in haematological parameters and the safety profile of Biobran (MGN-3) administered alongside conventional anticancer treatment in patients with haematological malignancies.

2.2 Study Population and Sampling

The expected sample size was 30 patients. However, a total of 22 patients with newly diagnosed haematological malignancies, enrolled between May and December 2024, were included in the final analysis using purposive sampling. Patients aged 18 years or older who received Biobran (MGN-3) alongside conventional anticancer treatment, provided informed consent, and had complete follow-up data were selected for analysis.

Patients with different haematological malignancies, including leukaemia, lymphoma, and multiple myeloma, were included. Patients receiving other investigational immunomodulatory therapies, those with active infections or autoimmune diseases requiring immunosuppressive treatment, pregnant or lactating women, and those with known hypersensitivity to rice-based compounds were excluded, in accordance with the proposed eligibility criteria.

2.3 Treatment and Follow-up

All participants received oral Biobran (MGN-3) at a dose of 1 g/day as an adjunct to their prescribed anticancer treatment. Conventional treatment was administered according to the underlying malignancy and included chemotherapy, targeted therapy, or immunotherapy, as appropriate. Supportive medications, including antibiotics, antifungal agents, and antiemetics, were administered when clinically indicated.

Patients were prospectively followed during treatment. Assessments were planned every two weeks during chemotherapy and every four weeks following chemotherapy, over one and half year period. Clinical and laboratory findings were recorded at the scheduled visits.

2.4 Data Collection and Study Variables

Data were collected using a structured data collection sheet. Baseline information included age, sex, residence, comorbidities, type of haematological malignancy, previous treatment history, and prescribed anticancer regimen.

Haematological parameters included red blood cell (RBC) count, haemoglobin concentration, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), absolute neutrophil count, lymphocyte count, monocyte count, eosinophil count, basophil count, and platelet count.

Liver function was assessed using serum bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase. Kidney function was evaluated using serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin-to-creatinine ratio (ACR).

Haematological abnormalities were defined using study-specific laboratory thresholds. Anaemia was defined as haemoglobin <10 g/dL and severe anaemia as <8 g/dL, corresponding to the haemoglobin criterion for CTCAE v5.0 grade 3 anaemia. Neutropenia was defined as an absolute neutrophil count <1.5 × 10⁹/L and severe neutropenia as <0.5 × 10⁹/LL, corresponding to CTCAE v5.0 grade 4. Thrombocytopenia was defined as a platelet count <100 × 10⁹/L and severe thrombocytopenia as <50 × 10⁹/L, corresponding to CTCAE v5.0 grades 3–4. Lymphopenia was defined as a lymphocyte count <1.0 × 10⁹/.These definitions were laboratory-based and did not constitute full clinical CTCAE grading [19].

Reported adverse events, including fever, diarrhoea, sore throat, oral mucositis or thrush, anorexia, alopecia, weight loss, and nausea or vomiting, were recorded during follow-up. Antibiotic or antifungal use and hospitalisation were also documented.

2.5 Outcome Measures

The primary outcome was the change in haematological parameters from baseline to the final follow-up visit.

Secondary outcomes included changes in liver and kidney function parameters, the frequency of cytopenias, and the occurrence of adverse events during treatment. Antibiotic or antifungal use and hospitalisation were also evaluated as indicators of clinical tolerability and supportive care requirements.

2.6 Statistical Analysis

Data were summarised using descriptive statistics. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages.

Changes in laboratory parameters between baseline and the final follow-up visit were assessed using the Wilcoxon signed-rank test. The Friedman test was used to evaluate differences in laboratory parameters across repeated follow-up visits. A p-value <0.05 was considered statistically significant.

2.7 Ethical Considerations

Written informed consent was obtained from all participants before inclusion in the study. Patient information was handled confidentially, and individual identities were not disclosed during data analysis or reporting.

3. Results

3.1 Sociodemographic characteristics

Table 1: Socio-demographic characteristics of the patients (n = 22)

Characteristic	n (%)
Age (years), mean ± SD	48.1 ± 15.2
Age group	
<30	3 (13.6)
30-44	6 (27.3)
45-59	6 (27.3)
≥60	7 (31.8)
Sex	
Male	14 (63.6)
Female	8 (36.4)
Residence	
Dhaka & surrounding	7 (31.8)
Outside Dhaka	15 (68.2)
Comorbidities	
None	8 (36.4)
Diabetes mellitus (DM)	4 (18.2)
Hypertension (HTN)	5 (22.7)
Bronchial asthma (BA)	7 (31.8)
≥2 comorbidities	2 (9.1)

Values are n (%) unless stated otherwise. SD, standard deviation.

Table 1 presents the sociodemographic characteristics of the 22 patients included in the study. The mean age was 48.1 ± 15.2 years, with the largest proportion aged ≥60 years (31.8%). Patients aged 30–44 and 45–59 years each accounted for 27.3%, while 13.6% were younger than 30 years. There was a male predominance, with 14 (63.6%) males and 8 (36.4%) females, giving a male-to-female ratio of 1.75:1. Most patients (68.2%) resided outside Dhaka, whereas 31.8% were from Dhaka and its surrounding areas.

Regarding comorbidities, 8 patients (36.4%) had no reported comorbid conditions. Bronchial asthma was the most frequently documented comorbidity (31.8%), followed by hypertension (22.7%) and diabetes mellitus (18.2%). Two patients (9.1%) had two or more comorbidities.

3.2 Clinical characteristics and treatment

Table 2: Clinical characteristics and treatment regimen of the patients (n = 22)

Characteristic	n (%)
Type of haematological malignancy	
Multiple myeloma	5 (22.7)
Diffuse large B-cell lymphoma (DLBCL)	5 (22.7)
Acute myeloid leukemia (AML)	3 (13.6)
Hodgkin lymphoma (classical)	3 (13.6)
Chronic myeloid leukemia (CML), chronic phase	2 (9.1)
Acute lymphoblastic leukemia (B-ALL)	2 (9.1)
Chronic lymphocytic leukemia (CLL)	2 (9.1)
Previous treatment	
None (newly diagnosed)	22 (100.0)
Histological grade	
Not reported / not applicable	17 (77.3)
High grade	5 (22.7)
Treatment regimen (all with Biobran MGN-3 1 g/day orally)	
Bortezomib + Lenalidomide + Dexamethasone (VRd)	5 (22.7)
R-CHOP	5 (22.7)
Cytarabine + Daunorubicin	3 (13.6)
ABVD	3 (13.6)
Imatinib	2 (9.1)
Hyper-CVAD (Part A)	2 (9.1)
Chlorambucil + Rituximab	2 (9.1)
Radiotherapy received	
No	22 (100.0)

Values are n (%) unless stated otherwise. ISS, International Staging System; ABVD, doxorubicin-bleomycin-vinblastine-dacarbazine; R-CHOP, rituximab-cyclophosphamide-doxorubicin-vincristine-prednisolone; VRd, bortezomib-lenalidomide-dexamethasone.

Table 2 summarises the clinical characteristics and treatment regimens of the participants. Multiple myeloma and diffuse large B-cell lymphoma (DLBCL) were the most common diagnoses, each affecting 5 patients (22.7%). Acute myeloid leukaemia (AML) and classical Hodgkin lymphoma were diagnosed in 3 patients (13.6%) each. Chronic-phase chronic myeloid leukaemia (CML), B-cell acute lymphoblastic leukaemia (B-ALL), and chronic lymphocytic leukaemia (CLL) each accounted for 2 patients (9.1%). All participants were newly diagnosed and had not received previous anticancer treatment. Histological grade was reported as high in 5 patients (22.7%), while it was not reported or not applicable in the remaining 17 patients (77.3%).

All patients received oral Biobran (MGN-3) at a dose of 1 g/day alongside conventional anticancer treatment appropriate for their underlying malignancy. The most frequently administered regimens were bortezomib, lenalidomide, and dexamethasone (VRd) and rituximab-based R-CHOP, each prescribed to 5 patients (22.7%). Cytarabine with daunorubicin and ABVD were each administered to 3 patients (13.6%). Imatinib, Hyper-CVAD (Part A), and chlorambucil with rituximab were each used in 2 patients (9.1%). None of the participants received radiotherapy.

3.3 Changes in haematological parameters

Table 3: Haematological parameters of the patients over time (n = 22)

Parameter	Visit 1 (baseline)	Visit 2	Visit 3	Visit 4	Visit 5	Change V1→V5	p (V1 vs V5)[a]	p (overall)[b]
RBC (×10¹²/L)	3.41 ± 0.63	3.29 ± 0.48	3.50 ± 0.37	3.67 ± 0.36	3.84 ± 0.38	+0.43	<0.001	<0.001
Haemoglobin (g/dL)	9.7 ± 1.6	9.5 ± 1.1	10.0 ± 0.8	10.6 ± 0.7	11.2 ± 0.7	+1.43	<0.001	<0.001
MCV (fL)	88.8 ± 3.9	89.3 ± 3.9	89.6 ± 3.9	90.1 ± 4.1	90.7 ± 4.2	+1.91	<0.001	<0.001
MCH (pg)	28.6 ± 1.6	28.7 ± 1.7	28.8 ± 1.8	29.0 ± 1.7	29.1 ± 1.8	+0.53	<0.001	<0.001
MCHC (g/dL)	32.2 ± 0.8	32.2 ± 0.8	32.2 ± 0.8	32.2 ± 0.8	32.1 ± 0.8	-0.06	0.593	0.883
Neutrophils (×10⁹/L) †	3.10 (2.29-4.16)	2.04 (1.75-2.40)	2.75 (2.36-3.17)	2.47 (2.10-2.93)	3.07 (2.85-3.38)	-0.18	0.187	<0.001
Lymphocytes (×10⁹/L) †	1.19 (1.02-2.04)	0.81 (0.60-1.21)	1.30 (1.02-1.43)	1.39 (0.92-1.71)	1.56 (1.12-1.79)	+0.10	0.910	<0.001
Monocytes (×10⁹/L)	0.52 ± 0.16	0.46 ± 0.29	0.55 ± 0.19	0.55 ± 0.21	0.61 ± 0.13	+0.09	0.039	0.320
Eosinophils (×10⁹/L)	0.16 ± 0.07	0.12 ± 0.09	0.16 ± 0.08	0.16 ± 0.07	0.17 ± 0.07	+0.01	0.385	0.076
Basophils (×10⁹/L)	0.03 ± 0.01	0.02 ± 0.02	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	-0.00	0.849	0.130
Platelets (×10⁹/L) †	202 (134-304)	150 (122-226)	175 (143-252)	182 (161-235)	208 (188-248)	-4.50	0.651	<0.001

Values are mean ± SD. † Skewed variable, shown as median (interquartile range). [a] Wilcoxon signed-rank test, baseline vs last visit. [b] Friedman test across all visits. $p < 0.05$ considered significant.

Table 3 presents changes in haematological parameters across five follow-up visits. Mean RBC count initially decreased from 3.41 ± 0.63 × 10¹²/L at baseline to 3.29 ± 0.48 × 10¹²/L at Visit 2, followed by a progressive increase to 3.84 ± 0.38 × 10¹²/L at Visit 5. The baseline-to-final increase was statistically significant ($p < 0.001$), as was the overall variation across visits ($p < 0.001$). A similar pattern was observed for haemoglobin, which decreased slightly from 9.7 ± 1.6 g/dL at baseline to 9.5 ± 1.1 g/dL at Visit 2 before increasing steadily to 10.0 ± 0.8, 10.6 ± 0.7, and 11.2 ± 0.7 g/dL at Visits 3, 4, and 5, respectively. Both the baseline-to-final change and overall variation were statistically significant ($p < 0.001$).

Red cell indices also showed changes during follow-up. Mean corpuscular volume (MCV) increased progressively from 88.8 ± 3.9 fL to 90.7 ± 4.2 fL, while mean corpuscular haemoglobin (MCH) increased from 28.6 ± 1.6 pg to 29.1 ± 1.8 pg. Both parameters demonstrated statistically significant changes between baseline and the final visit and across all visits ($p < 0.001$). In contrast, mean corpuscular haemoglobin concentration (MCHC) remained relatively stable, with no significant baseline-to-final difference ($p = 0.593$) or overall variation ($p = 0.883$).

White blood cell subpopulations showed variable trends. Median neutrophil count decreased from 3.10 × 10⁹/L at baseline to 2.04 × 10⁹/L at Visit 2, followed by fluctuations and recovery to 3.07 × 10⁹/L at Visit 5. Although the overall variation was statistically significant ($p < 0.001$), the baseline-to-final difference was not significant ($p = 0.187$). Median lymphocyte count similarly decreased from 1.19 × 10⁹/L at baseline to 0.81 × 10⁹/L at Visit 2 before increasing to 1.56 × 10⁹/L at the final visit. The overall variation was significant ($p < 0.001$), whereas the baseline-to-final comparison was not ($p = 0.910$).

Mean monocyte count increased from 0.52 ± 0.16 × 10⁹/L at baseline to 0.61 ± 0.13 × 10⁹/L at Visit 5, with a significant baseline-to-final difference ($p = 0.039$), although the overall variation was not significant ($p = 0.320$). Eosinophil and basophil counts remained relatively stable throughout follow-up, without statistically significant changes. Median platelet count decreased from 202 × 10⁹/L at baseline to 150 × 10⁹/L at Visit 2, followed by gradual recovery to 208 × 10⁹/L at Visit 5. The overall variation was statistically significant ($p < 0.001$), but the baseline-to-final difference was not ($p = 0.651$).

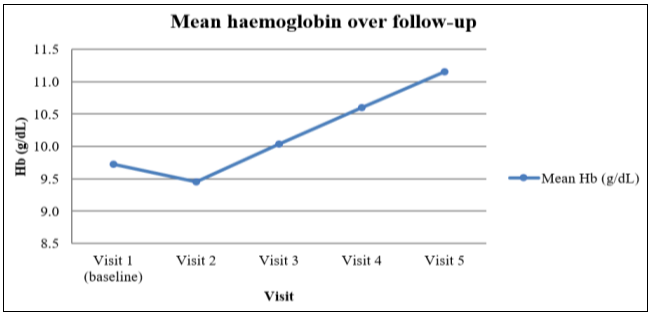


Fig 1: Trends in mean haemoglobin concentration over time (n=22)

Fig 1 illustrates the changes in mean haemoglobin concentration across the five visits. An initial decline was observed at Visit 2, followed by a consistent increase during subsequent assessments. The mean haemoglobin level reached its highest value at Visit 5 (11.2 g/dL), compared with 9.7 g/dL at baseline, demonstrating an overall improvement during follow-up.

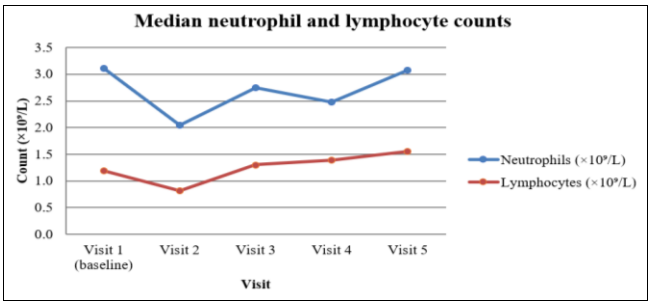


Fig 2: Trends in median neutrophil and lymphocyte counts over time (n=22)

Fig 2 illustrates the trends in median neutrophil and lymphocyte counts across the five visits. Both parameters decreased at Visit 2, followed by subsequent recovery. Neutrophil counts fluctuated during the intermediate visits before approaching baseline levels at the final assessment. Lymphocyte counts increased after Visit 2 and reached their highest median value at Visit 5. These trends reflect variations in circulating leukocyte counts during the observation period.

3.4 Changes in liver and kidney function parameters

Table 4: Trends in liver and kidney function tests over time (n = 22)

Parameter	Visit 1 (baseline)	Visit 2	Visit 3	Visit 4	Change V1→V4	p (V1 vs V4)[a]	p (overall)[b]
Serum bilirubin (mg/dL)	0.69 ± 0.08	0.89 ± 0.16	0.71 ± 0.10	0.77 ± 0.07	+0.08	0.003	<0.001
Serum albumin (g/dL)	3.42 ± 0.11	3.46 ± 0.13	3.59 ± 0.08	3.73 ± 0.10	+0.31	<0.001	<0.001
SGPT/ALT (U/L)	28 ± 3	35 ± 11	29 ± 6	30 ± 4	+1.82	0.110	0.004
SGOT/AST (U/L)	27 ± 3	33 ± 8	27 ± 5	29 ± 4	+2.82	0.018	<0.001
Alkaline phosphatase (U/L)	104 ± 10	104 ± 13	104 ± 10	101 ± 10	-3.32	0.242	0.081
Serum creatinine (mg/dL)	1.05 ± 0.24	1.02 ± 0.19	1.00 ± 0.16	0.97 ± 0.15	-0.08	0.024	0.115
eGFR (mL/min/1.73 m²)	85 ± 24	87 ± 22	87 ± 22	90 ± 22	+4.50	0.032	0.147
Urine ACR (mg/g)	28 ± 21	29 ± 21	24 ± 16	25 ± 17	-2.41	0.360	0.094

Values are mean ± SD. [a] Wilcoxon signed-rank test, baseline vs last visit. [b] Friedman test across all visits. SGPT, serum glutamic pyruvic transaminase; SGOT, serum glutamic oxaloacetic transaminase; eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio.

Table 4 summarises changes in liver and kidney function parameters across four follow-up visits. Mean serum bilirubin increased from 0.69 ± 0.08 mg/dL at baseline to 0.89 ± 0.16 mg/dL at Visit 2, subsequently decreasing to 0.71 ± 0.10 mg/dL at Visit 3 and reaching 0.77 ± 0.07 mg/dL at Visit 4. Both the baseline-to-final difference ($p = 0.003$) and overall variation ($p < 0.001$) were statistically significant. Serum albumin increased progressively from 3.42 ± 0.11 g/dL at baseline to 3.73 ± 0.10 g/dL at the final assessment, with significant baseline-to-final and overall changes (both $p < 0.001$).

Regarding liver enzymes, mean alanine aminotransferase (ALT) increased from 28 ± 3 U/L at baseline to 35 ± 11 U/L at Visit 2 before decreasing to 29 ± 6 U/L and 30 ± 4 U/L at Visits 3 and 4, respectively. Although the overall variation was significant ($p = 0.004$), the baseline-to-final difference was not statistically significant ($p = 0.110$). Mean aspartate aminotransferase (AST) showed a similar early increase from 27 ± 3 U/L to 33 ± 8 U/L at Visit 2, followed by a decrease to 27 ± 5 U/L at Visit 3 and 29 ± 4 U/L at Visit 4. Both the baseline-to-final difference ($p = 0.018$) and overall variation ($p < 0.001$) were significant. Alkaline phosphatase remained relatively stable, decreasing slightly from 104 ± 10 U/L to 101 ± 10 U/L, without significant changes.

Renal function parameters showed modest changes during follow-up. Mean serum creatinine decreased progressively from 1.05 ± 0.24 mg/dL at baseline to 0.97 ± 0.15 mg/dL at Visit 4, with a significant baseline-to-final difference ($p = 0.024$), although the overall variation was not significant ($p = 0.115$). Mean estimated glomerular filtration rate (eGFR) increased from 85 ± 24 to 90 ± 22 mL/min/1.73 m², with a significant baseline-to-final difference ($p = 0.032$) but no significant overall variation ($p = 0.147$). Urine albumin-to-creatinine ratio (ACR) decreased from 28 ± 21 to 25 ± 17 mg/g, although neither the baseline-to-final difference ($p = 0.360$) nor the overall variation ($p = 0.094$) was statistically significant.

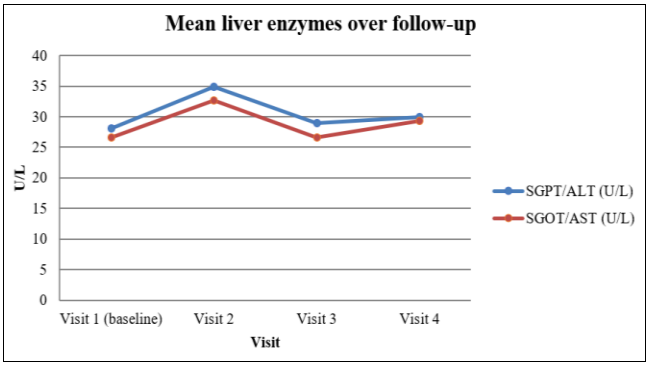


Fig 3: Trends in mean ALT and AST concentration over time (n=22)

Fig 3 illustrates the changes in mean ALT and AST concentrations across the four visits. Both enzymes increased at Visit 2, with ALT rising from 28 to 35 U/L and AST from 27 to 33 U/L. Subsequently, both parameters decreased towards their baseline values. At the final assessment, mean ALT and AST levels were 30 and 29 U/L, respectively. Thus, the figure demonstrates an early increase in liver enzyme concentrations followed by a reduction during subsequent visits.

3.5 Frequency of cytopenias during follow-up

Table 5: Proportion of patients with cytopenia at each visit (n = 22)

Cytopenia	Visit 1 (baseline)	Visit 2	Visit 3	Visit 4	Visit 5
Anaemia (Hb <10 g/dL)	12 (54.5)	15 (68.2)	11 (50.0)	4 (18.2)	1 (4.5)
Severe anaemia (Hb <8 g/dL)	4 (18.2)	3 (13.6)	0 (0.0)	0 (0.0)	0 (0.0)
Neutropenia (ANC <1.5 ×10⁹/L)	5 (22.7)	5 (22.7)	2 (9.1)	2 (9.1)	0 (0.0)
Severe neutropenia (ANC <0.5 ×10⁹/L)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombocytopenia (platelets <100 ×10⁹/L)	5 (22.7)	5 (22.7)	0 (0.0)	2 (9.1)	0 (0.0)
Severe thrombocytopenia (platelets <50 ×10⁹/L)	5 (22.7)	5 (22.7)	0 (0.0)	0 (0.0)	0 (0.0)
Lymphopenia (lymphocytes <1.0 ×10⁹/L)	5 (22.7)	14 (63.6)	3 (13.6)	7 (31.8)	4 (18.2)

Values are n (%). ANC, absolute neutrophil count.

Table 5 presents the frequency of cytopenias across the five visits. Anaemia, defined as haemoglobin <10 g/dL, was present in 12 patients (54.5%) at baseline and increased to 15 patients (68.2%) at Visit 2. Thereafter, its frequency declined progressively to 11 patients (50.0%) at Visit 3, 4 patients (18.2%) at Visit 4, and 1 patient (4.5%) at Visit 5. Severe anaemia (haemoglobin <8 g/dL) was observed in 4 patients (18.2%) at baseline and 3 patients (13.6%) at Visit 2 but was not reported during subsequent visits.

Neutropenia, defined as an absolute neutrophil count <1.5 × 10^9/L, was present in 5 patients (22.7%) at both baseline and Visit 2. Its frequency decreased to 2 patients (9.1%) at Visits 3 and 4, and no cases were reported at the final visit. Severe neutropenia (<0.5 × 10^9/L) was not observed at any assessment. Similarly, thrombocytopenia (platelet count <100 × 10^9/L) was recorded in 5 patients (22.7%) at baseline and Visit 2. No cases were reported at Visit 3, although 2 patients (9.1%) had thrombocytopenia at Visit 4. No thrombocytopenia was observed at Visit 5. Severe thrombocytopenia (platelet count <50 × 10^9/L) was present in 5 patients (22.7%) at baseline and Visit 2 but was absent during subsequent visits.

Lymphopenia, defined as a lymphocyte count <1.0 × 10^9/L, demonstrated a more variable pattern. It was present in 5 patients (22.7%) at baseline and increased markedly to 14 patients (63.6%) at Visit 2. Its frequency subsequently decreased to 3 patients (13.6%) at Visit 3, increased to 7 patients (31.8%) at Visit 4, and declined to 4 patients (18.2%) at Visit 5. Overall, anaemia, neutropenia, and thrombocytopenia were less frequent at the final visit than at baseline, while lymphopenia continued to be observed in a small proportion of patients.

3.6 Reported adverse events and supportive care

Table 6: Adverse effects reported at each visit (n = 22)

Adverse effect	Visit 1 (baseline)	Visit 2	Visit 3	Visit 4	Any time during follow-up
Fever	1 (4.5)	4 (18.2)	2 (9.1)	2 (9.1)	7 (31.8)
Diarrhoea	1 (4.5)	7 (31.8)	1 (4.5)	2 (9.1)	10 (45.5)
Sore throat	0 (0.0)	3 (13.6)	1 (4.5)	2 (9.1)	6 (27.3)
Oral mucositis / thrush	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.5)	1 (4.5)
Anorexia	10 (45.5)	7 (31.8)	3 (13.6)	2 (9.1)	15 (68.2)
Alopecia	0 (0.0)	13 (59.1)	13 (59.1)	13 (59.1)	13 (59.1)
Weight loss	9 (40.9)	4 (18.2)	3 (13.6)	1 (4.5)	14 (63.6)
Nausea / vomiting	0 (0.0)	11 (50.0)	8 (36.4)	7 (31.8)	16 (72.7)
Antibiotic / antifungal use	1 (4.5)	4 (18.2)	2 (9.1)	2 (9.1)	7 (31.8)
Hospitalisation	0 (0.0)	4 (18.2)	0 (0.0)	1 (4.5)	4 (18.2)

Values are n (%). 'Any time' counts each patient once if the effect was reported at one or more visits.

Table 6 presents the frequency of reported adverse events, antibiotic or antifungal use, and hospitalisation during follow-up. Nausea or vomiting was the most frequently reported event, affecting 16 patients (72.7%) at least once during the observation period. It was not reported at baseline but occurred in 11 patients (50.0%) at Visit 2, 8 patients (36.4%) at Visit 3, and 7 patients (31.8%) at Visit 4. Anorexia was reported in 15 patients (68.2%) at any time, with its frequency decreasing from 10 patients (45.5%) at baseline to 2 patients (9.1%) at Visit 4. Weight loss affected 14 patients (63.6%) at least once and similarly became less frequent across the recorded visits, declining from 40.9% at baseline to 4.5% at Visit 4.

Alopecia was reported in 13 patients (59.1%) during follow-up. It was absent at baseline but was recorded in the same number of patients at Visits 2, 3, and 4. Diarrhoea affected 10 patients (45.5%) at any time, with the highest frequency at Visit 2 (31.8%), followed by lower frequencies at subsequent assessments. Fever was reported in 7 patients (31.8%) during the observation period, while sore throat occurred in 6 patients (27.3%). Oral mucositis or thrush was uncommon, affecting only 1 patient (4.5%) at Visit 4.

Antibiotic or antifungal use was recorded in 7 patients (31.8%) at least once during follow-up. Its frequency was highest at Visit 2, when 4 patients (18.2%) received these medications. Hospitalisation was required in 4 patients (18.2%) during the observation period, with 4 hospitalisation reports at Visit 2 and 1 at Visit 4. As the table records patients affected at each visit and the number affected at any time, these findings do not establish the number of separate hospitalisation episodes. Overall, gastrointestinal symptoms, alopecia, and constitutional symptoms were commonly reported during combined treatment, while oral mucositis or thrush was relatively uncommon.

4. Discussion

The present study evaluated haematological changes and laboratory safety findings among 22 patients with haematological malignancies receiving Biobran (MGN-3) alongside conventional anticancer treatment. Significant improvements were observed in haemoglobin and RBC counts during follow-up, accompanied by a reduction in the frequency of anaemia. Neutrophil, lymphocyte, and platelet counts showed significant fluctuations across visits, although their final values were not significantly different from baseline. Liver and kidney function parameters demonstrated relatively modest changes, while several adverse events were reported during treatment.

The improvement in haemoglobin was one of the principal findings of this study. Mean haemoglobin increased from 9.7 ± 1.6 g/dL at baseline to 11.2 ± 0.7 g/dL at the final visit ($p < 0.001$). Similarly, RBC counts increased significantly, while the proportion of patients with anaemia decreased from 54.5% to 4.5%. These findings indicate haematological improvement during the observation period. Cancer-associated anaemia may result from multiple factors, including bone marrow involvement, inflammation, nutritional deficiencies, and anticancer treatment [1-3]. Although previous investigations have demonstrated the immunomodulatory properties of Biobran [12, 13], evidence supporting its direct effects on erythropoiesis remains insufficient. Therefore, the observed improvement in haemoglobin may also reflect disease control, bone marrow

recovery, or supportive treatment.

Neutrophil, lymphocyte, and platelet counts showed significant variations throughout follow-up, with an initial decline in several parameters followed by subsequent recovery. However, baseline-to-final comparisons were not statistically significant. These fluctuations may be related to the underlying malignancies and their respective treatment regimens. In a randomized placebo-controlled study involving 48 patients with multiple myeloma, Cholujova *et al*. [12] reported increased NK cell activity, changes in dendritic cell populations, and increased concentrations of selected cytokines following MGN-3 administration. Similarly, Elsaid *et al*. [13] demonstrated increased NK cell activity among older adults receiving Biobran supplementation. Experimental investigations have also demonstrated effects of MGN-3 on dendritic cell activation, cytotoxic T-cell responses, and phagocytic activity [8, 10, 11]. Although these findings suggest potential immunomodulatory activity, the present study did not directly assess immune cell function or cytokine responses. Consequently, changes in circulating leukocyte counts cannot be interpreted as evidence of enhanced immune activity.

Experimental studies have additionally explored the potential interaction of MGN-3 with malignant cells and anticancer agents. Ghoneum and Gollapudi [20] demonstrated increased susceptibility of human T-cell leukaemia cells to death receptor-mediated apoptosis following MGN-3 exposure. Another laboratory investigation reported enhanced sensitivity of breast cancer cells to paclitaxel in the presence of MGN-3 [21]. Although these findings provide a possible biological rationale for further investigation, they were obtained under experimental conditions and cannot establish clinical efficacy or improved treatment tolerability in patients with haematological malignancies.

The frequency of cytopenias also changed during follow-up. Anaemia, neutropenia, and thrombocytopenia were less frequently observed at the final visit than at baseline, while severe anaemia and severe thrombocytopenia were not reported during later assessments. These findings are clinically relevant because cytopenias are common complications of haematological malignancies and anticancer treatment. Chemotherapy-induced thrombocytopenia may increase bleeding risk and contribute to treatment delays or dose reductions [4]. Similarly, neutropenia increases susceptibility to infection, and febrile neutropenia remains an important complication requiring prompt clinical assessment and treatment [5, 22]. Nevertheless, the reduction in cytopenias observed in the present study cannot be attributed specifically to Biobran, particularly because patients received different anticancer regimens.

Laboratory safety was evaluated through repeated assessments of liver and kidney function. Serum bilirubin and AST increased significantly between baseline and the final assessment, although the absolute changes were modest. ALT showed variations during follow-up but did not differ significantly between baseline and the final visit. Serum albumin increased significantly, while alkaline phosphatase remained relatively stable. Regarding renal parameters, serum creatinine decreased modestly and eGFR increased, whereas urine ACR showed no significant change. Elsaid *et al*. [13] also assessed selected laboratory parameters during Biobran supplementation and reported no major safety concerns over their short observation period. However, the present findings should be interpreted cautiously because concurrent anticancer treatment, supportive medications, and disease-related factors may influence liver and kidney function. The evaluation of suspected treatment-related liver injury requires consideration of the magnitude and pattern of laboratory abnormalities, together with the clinical context [23]. Furthermore, group-level laboratory values cannot exclude clinically important abnormalities in individual patients.

Clinical tolerability was assessed through reported adverse events, supportive medication use, and hospitalisation. Nausea or vomiting, anorexia, weight loss, alopecia, and diarrhoea were frequently reported during follow-up. Fever and sore throat were also observed, while oral mucositis or thrush was uncommon. Antibiotic or antifungal use was reported in 31.8% of patients, and 18.2% required hospitalisation. These events occurred during combined treatment and may be associated with the underlying malignancies, conventional anticancer regimens, or other clinical factors. Fever and infection-related complications are particularly important among patients receiving myelosuppressive chemotherapy [22, 24]. Ooi *et al*. [6], in their evidence-based review, identified potential supportive benefits of Biobran but emphasised the limited size and duration of available clinical studies. More recent investigations have explored patient-reported outcomes during adjunctive rice bran arabinoxylan administration, although differences in study populations and treatment regimens limit direct comparison with the present findings [17, 18]. Thus, the present study provides additional descriptive information on clinical tolerability, but the absence of a comparator group prevents assessment of Biobran-specific adverse effects.

This study has several limitations. The single-center design and small sample size limit the generalisability and statistical precision of the findings. Patients had different haematological malignancies and received heterogeneous anticancer regimens, which may have influenced haematological recovery and treatment-related complications. Purposive sampling and inclusion of only patients with complete follow-up data may have introduced selection bias. Furthermore, the absence of a control group prevents determination of the independent contribution of Biobran to the observed outcomes. Immune function was not directly assessed, and adverse events were not evaluated for their causal relationship with Biobran. Finally, multiple statistical comparisons were performed, increasing the possibility of chance findings.

Despite these limitations, the prospective collection of serial haematological, hepatic, renal, and clinical data provides a useful description of changes observed during adjunctive Biobran administration. Larger controlled studies involving more homogeneous patient populations are needed to clarify its potential clinical benefits and safety in patients with haematological malignancies.

5. Conclusion

Patients with haematological malignancies receiving Biobran (MGN-3) alongside conventional anticancer treatment showed significant improvements in haemoglobin and RBC counts, with a reduction in the frequency of cytopenias during follow-up. Liver and kidney function parameters showed relatively modest changes, while several

adverse events were reported during treatment. Although these findings provide preliminary information on haematological changes and laboratory safety during adjunctive Biobran administration, its independent effects could not be established. Larger controlled studies are needed to evaluate its efficacy and safety in this patient population.

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