

Impact of Shenling Baizhu Powder on lipid profiles and body mass index in breast cancer patients under adjuvant chemotherapy: a retrospective study

Jiaqing Song^{1#}^, Ying Jin^{1#}^, Qinghong Yu¹^, Hongting Wu¹^, Hailong Li²^, Geok Hoon Lim³, Marcelo Antonini⁴^, Xiufei Gao⁵^

¹The First School of Clinical Medicine, Zhejiang Chinese Medical University, Hangzhou, China; ²School of Green Intelligent Pharmaceutical, Zhejiang Guangsha Vocational and Technical University of Construction, Jinhua, China; ³Breast Department, KK Women's and Children's Hospital, Singapore, Singapore, ⁴Department of Breast Surgery, Hospital do Servidor Público Estadual (HSPE), São Paulo, Brazil; ⁵Department of Breast Disease Center, The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine), Hangzhou, China

Contributions: (I) Conception and design: J Song, Y Jin; (II) Administrative support: X Gao; (III) Provision of study materials or patients: X Gao; (IV) Collection and assembly of data: Q Yu, H Wu, H Li; (V) Data analysis and interpretation: J Song, Y Jin; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

*These authors contributed equally to this work as co-first authors.

Correspondence to: Xiufei Gao, MD. Department of Breast Disease Center, The First Affiliated Hospital of Zhejiang Chinese Medical University (Zhejiang Provincial Hospital of Traditional Chinese Medicine), No. 54 Youdian Road, Hangzhou 310006, China. Email: gaoxiufei@zcmu.edu.cn.

Background: Breast cancer is the second most common cancer worldwide. Chemotherapy often causes dyslipidemia and obesity in breast cancer patients. Monitoring lipid profiles and body mass index (BMI) is crucial to evaluate chemotherapy's metabolic side effects, identify interventions to mitigate them, and understand health risks linked to weight changes during treatment. Shenling Baizhu Powder (SLBZP), a traditional Chinese medicine (TCM), treats spleen-stomach ailments by boosting spleen function, enhancing qi, and reducing dampness. SLBZP has potential benefits in managing chemotherapy-induced dyslipidemia and improving overall metabolic health in cancer patients. This study retrospectively examined the effects of SLBZP on blood lipid levels and BMI in breast cancer patients undergoing adjuvant chemotherapy.

Methods: This study reviewed the medical records of patients who were diagnosed with breast cancer at the Breast Surgery Department of Zhejiang Provincial Hospital of Traditional Chinese Medicine from January 2022 to December 2023. Based on the inclusion criteria, a total of 180 eligible patients were included and divided into an observational group (which received SLBZP) and a control group (which did not receive SLBZP) during chemotherapy. Patients' clinical data, including age at diagnosis, menopausal status, tumor location, smoking and drinking habits, tumor molecular type, tumor node metastasis (TNM) stage, chemotherapy drugs, targeted therapy, lipid levels, and BMI before and after chemotherapy, were collected. Statistical analyses were conducted using SPSS 25.0.

Results: After chemotherapy, the control group showed significant increases in total cholesterol (TC) (P=0.03), triglyceride (TG) (P=0.001), low-density lipoprotein cholesterol (LDL-C) (P=0.02), and apolipoprotein B (ApoB) (P=0.01) levels. In the observational group, the TC, TG, and LDL-C levels remained stable (P>0.05), but the high-density lipoprotein cholesterol (HDL-C) (P=0.001) and apolipoprotein A1 (ApoA1) (P<0.001) levels significantly decreased, and BMI (P=0.02) significantly increased. The subgroup analysis revealed that the taxane followed by anthracycline subgroup showed significant increases in BMI (P=0.007) and significant decreases in the HDL-C (P=0.007) and ApoA1 (P<0.001) levels,

[^] ORCID: Jiaqing Song, 0000-0002-8281-407X; Ying Jin, 0009-0003-8208-1149; Qinghong Yu, 0000-0003-0710-8383; Hongting Wu, 0009-0006-3730-4560; Hailong Li, 0000-0001-7781-6815; Marcelo Antonini, 0000-0002-1996-7428; Xiufei Gao, 0000-0002-2560-7920.

while the taxane subgroup showed a significant decrease in the HDL-C level post-chemotherapy (P=0.003). In the control group, the TG (P=0.002) and LDL-C (P=0.02) levels were significantly elevated in the taxane followed by anthracycline subgroup post-chemotherapy. No significant changes were observed in BMI or the other lipid indexes in the remaining chemotherapy drug regime subgroups (P>0.05).

Conclusions: Chemotherapy increased the TC, TG, LDL-C, and ApoB levels in breast cancer patients, but SLBZP mitigated dyslipidemia. The patients who received SLBZP also showed increased BMI post-chemotherapy, which was likely due to reduced gastrointestinal side effects. Taxane-based chemotherapy drugs had greater effects on blood lipids and BMI, while anthracycline-based drugs did not significantly affect blood lipids and BMI.

Keywords: Shenling Baizhu Powder (SLBZP); breast cancer; adjuvant chemotherapy; blood lipids; body mass index (BMI)

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Introduction

According to the most recent data published by the International Agency for Research on Cancer, the global incidence of this disease reached 2.3 million cases in 2022,

Highlight box

Key findings

- Shenling Baizhu Powder (SLBZP) could mitigate dyslipidemia arising as a result of chemotherapy in breast cancer patients.
- Patients treated with SLBZP experienced increased body mass index (BMI) after chemotherapy, likely due to fewer gastrointestinal side effects.
- Taxane-based chemotherapy significantly impacted blood lipids and BMI, whereas anthracycline-based drugs did not.

What is known, and what is new?

- Chemotherapy has been shown to induce dyslipidemia in breast cancer patients, and is characterized by significant increases in total cholesterol, triglyceride, low density lipoprotein cholesterol, and apolipoprotein B levels. SLBZP is a traditional Chinese medicine used for treating spleen-stomach ailments.
- We aimed to investigate the effects of SLBZP on the lipid profiles and BMI of breast cancer patients undergoing chemotherapy.

What is the implication, and what should change now?

 These findings could help to minimize the adverse effects of chemotherapy on the lipid profiles of breast cancer patients.
 Future studies will need to be undertaken to investigate further the effects of SLBZP on lipid metabolism, endothelial dysfunction, and cytokine alterations induced by chemotherapy, and explore the mechanisms by which SLBZP mitigates the chemotherapy-induced dyslipidemia. making it the second most common cancer worldwide (1). Furthermore, breast cancer has overtaken gastric cancer to become the fourth leading cause of cancer-related death worldwide (1). In China, there were approximately 357,200 new cases of breast cancer in women in 2022, making it the fifth most common cancer (2). Additionally, breast cancer has surpassed colorectal cancer to become the fifth leading cause of cancer-related death among women in China (3).

Adjuvant chemotherapy, a common treatment modality for breast cancer, has been shown to prolong patient survival; however, it also induces alterations in blood lipid profiles (4). For instance, Ma et al. found that chemotherapy increased triglyceride (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C) levels, while decreasing high-density lipoprotein cholesterol (HDL-C) levels in breast cancer patients (5). Dyslipidemia has been implicated in the development of cardiovascular diseases and diabetes (6,7), which significantly compromises the quality of life and prognosis of breast cancer patients (8). Notably, LDL-C is recognized as a pathogenic risk factor for atherosclerotic cardiovascular diseases (9). Monitoring lipid profiles is essential to assess the metabolic side effects of chemotherapy and to identify potential interventions that can mitigate these effects. Obesity is an established risk factor for breast cancer in postmenopausal women (10), and serves as an independent poor prognostic factor for breast cancer patients, contributing to its increased incidence recurrence, and mortality rates (4,11). Body mass index (BMI) is a widely used indicator of overall health and metabolic status. Changes in BMI can reflect alterations in body composition and metabolic health,

which are important considerations in the management of chronic diseases, including cancer. Therefore, monitoring BMI is crucial for understanding the overall health status and potential risks associated with weight changes during chemotherapy. Furthermore, for patients exhibiting human epidermal growth factor receptor 2 (HER2) overexpression, targeted therapy is frequently administered in conjunction with chemotherapy. However, there is a lack of research investigating the effects of targeted therapy on blood lipid levels.

Shenling Baizhu Powder (SLBZP), a classical prescription in traditional Chinese medicine (TCM), originated from the Taiping Huimin Heji Ju Fang. It is known for its functions of invigorating the spleen, enhancing qi, reducing water retention, and alleviating dampness, with its primary action sites being the spleen and stomach. Research conducted by Li et al. identified the main chemical constituents of SLBZP as flavonoids, organic acids, terpenoids, and coumarin compounds (12). In the blood components, apigenin-7-O-glucoside, glycyrrhizin, orientin, daidzein, licoriphenone, and isoschaftoside were identified as flavonoids, glyvunnansapogenin E as a terpenoid, protocatechuic acid as an organic acid, and licocoumarone as a coumarin (12). Currently, SLBZP is used in the treatment of gastrointestinal diseases such as ulcerative colitis (13) and diarrhea (14,15). Additionally, studies have shown that SLBZP exerts protective effects against nonalcoholic fatty liver disease (16), and ameliorates metabolic correlations associated with fatty liver disease (17). Wang examined the combination of SLBZP and insulin aspart 30 in the treatment of type 2 diabetes mellitus, and found that this combination enhanced therapeutic efficacy, and regulated both blood glucose and lipid levels (18). In summary, existing evidence suggests that SLBZP has potential benefits in managing chemotherapy-induced dyslipidemia and improving overall metabolic health in cancer patients. However, few studies have investigated the effects of SLBZP on blood lipid levels and BMI in breast cancer patients undergoing adjuvant chemotherapy.

Thus, we conducted a retrospective study to examine the effects of SLBZP on blood lipid levels and BMI in patients undergoing adjuvant chemotherapy for breast cancer. We also examined the effects of different chemotherapy regimens and the use of targeted therapies on these parameters. We present this article in accordance with the STROBE reporting checklist (available at https://tcr. amegroups.com/article/view/10.21037/tcr-2024-2658/rc).

Methods

Study design

This study was designed as a retrospective observational study. Medical records of patients diagnosed with breast cancer between January 2022 and December 2023 were reviewed. The aim was to assess the changes in blood lipid levels and BMI associated with adjuvant chemotherapy and targeted therapy in patients with or without SLBZP. Patients were further stratified into groups based on their chemotherapy regimens and the use of targeted therapy. The observational nature of the study enabled the analysis of real-world data, providing insights into the biochemical and metabolic impacts of cancer treatments. No interventions were implemented as part of the study, and the data were analyzed retrospectively.

Subject enrollment

This study retrospectively reviewed the medical records of all patients who had been diagnosed with breast cancer at the Breast Surgery Department of Zhejiang Provincial Hospital of Traditional Chinese Medicine from January 2022 to December 2023.

To be eligible for inclusion in this study, the patients had to meet the following inclusion criteria: (I) be female and aged 18 years or older; (II) have undergone surgical treatment and received a pathological diagnosis of breast cancer; (III) have clinical stage I to III; and (IV) have received adjuvant chemotherapy post-surgery. Patients were excluded from the study if they met any of the following exclusion criteria: (I) had other malignant tumors; (II) had received neoadjuvant chemotherapy; (III) were pregnant or lactating; (IV) had diabetes; (V) were taking drugs that affect blood lipids (e.g., statins); (VI) with allergy to Chinese herbal medicine or severe hepatic and renal insufficiency; and/or (VII) had incomplete data.

Data collection

All the clinicopathological data were extracted from medical records. The clinical data collected included age at diagnosis, menopausal status, tumor location, smoking status, alcohol consumption, tumor molecular typing, tumor node metastasis (TNM) staging, types of chemotherapy agents administered, targeted therapy, BMI, and lipid levels measured both before the first chemotherapy cycle and after

the final chemotherapy cycle. According to the Chinese Guideline for Lipid Management (Primary Care Version 2024) (9), the biochemical indicators associated with dyslipidemia were classified using the following threshold values: TC: 5.2 mmol/L; TG: 1.7 mmol/L; LDL-C: 3.4 mmol/L; and HDL-C: 1.0 mmol/L. Dyslipidemia was diagnosed if a patient met at least one of the following criteria: TG \geq 1.7 mmol/L; TC \geq 5.2 mmol/L; LDL-C \geq 3.4 mmol/L; or HDL-C \leq 1.0 mmol/L. BMI was determined based on weight and height, and calculated as weight divided by the square of height (kg/m²). According to the World Health Organization in 2024, the most recent standards define a BMI of 25 kg/m² or higher as indicative of an overweight status in adults, and a BMI of 30 kg/m² or higher as indicative of obesity.

Reagents and drugs

The composition of SLBZP was as follows: dried tuber roots of Pseudostellaria heterophylla (Miq.) Pax ex Pax et Hoffm. (10 g), dried sclerotiums of Poria cocos (Schw.) Wolf (15 g), dried rhizomes of Atractylodes macrocephala Koidz. (10 g), dried rhizomes of Dioscorea opposita Thunb. (12 g), dried ripe seeds of Lablab purpureus (L.) Sweet (9 g), dried ripe seeds of Nelumbo nucifera Gaertn. (9 g), dried ripe seed kernel of Coix lacryma-jobi L. var. ma-yuen (Roman.) Stapf (15 g), dried ripe fruit of Amomum villosum Lour. (3 g), dried roots of Platycodon grandiflorum (Jacq.) A. DC. (9 g), and dried roots and rhizomes of Glycyrrhiza uralensis Fisch. (5 g).

All the Chinese medicinal preparations used in this study were Chinese herbal decoction pieces, uniformly distributed by the pharmacy of Zhejiang Provincial Hospital of Traditional Chinese Medicine. Chinese herbal decoction pieces are designated by the same manufacturer to ensure the consistency of varieties, producing areas, quality and processing methods. Choose manufacturers with standardized production operation, rigorous control science and good reputation. All the medicinal materials are packaged independently, and the packaging is printed with the source, product name, specifications, producing area, validity and other relevant information. The TCM decoction followed the standards established by the State Administration of TCM in accordance with the Ministry of Health's "Management Norms for Chinese Medicine Tisanes Room of Medical Institutions". Consequently, we ensured the standardization of the TCM decoction process. In order to maintain the stability and efficacy of herbal

solutions, the recommended storage temperature for herbal solutions is 2–8 °C, which can be stored for 2 weeks. For patients who opted for self-decoction, we mandated strict adherence to the established protocol. The following steps were employed:

- (I) Tisane containers made of materials such as ceramic, stainless steel, or copper were selected for use, and iron vessels, which are prone to corrosion, were not used;
- (II) Using the prescribed medicinal piece, the package was opened, and the content was soaked for approximately 30 minutes;
- (III) For the first decoction, water was added until it covered the surface of the medicine by 4–5 cm. After bringing the mixture to a boil, the heat was reduced to a low setting, and maintained at a gentle simmer, and the decoction process was continued for 60 minutes. The herbs were stirred 2–3 times during this period. On completion, the decoction was stopped, and the liquid was filtered into a clean container (no less than 200 mL);
- (IV) For the second decoction, water was added until it covered the surface of the medicinal ingredients by 1–2 cm. The mixture was brought to a boil, and the heat was then reduced to maintain a gentle simmer, and the decoction was continued for an additional 30 minutes, during which time, the mixture was stirred 2–3 times. On completion, the decoction was stopped, and the liquid was filtered into a clean container, ensuring that the final volume of the decoction was not less than 200 mL. The two potions were combined, and the mixture was concentrated to 400 mL using a potion pot;
- (V) The solution (200 mL) was administered twice daily, half an hour after meals in the morning and evening, at a warm temperature.

The breast cancer guidelines established by the Chinese Society of Clinical Oncology (19) recommended the following chemotherapy regimens:

- (I) Paclitaxel combined with cyclophosphamide (P: 175 mg/m², C: 600 mg/m²), administered every three weeks for 4–6 cycles;
- (II) Doxorubicin combined with cyclophosphamide (A: 60 mg/m², C: 600 mg/m²), administered every three weeks for 4 cycles;
- (III) Docetaxel combined with cyclophosphamide (T: 75 mg/m², C: 600 mg/m²), administered every three weeks for 4–6 cycles;

- (IV) Epirubicin or doxorubicin combined with cyclophosphamide (E: 90 mg/m², A: 60 mg/m², C: 600 mg/m²), followed by paclitaxel (P: 175 mg/m²) or docetaxel (T: 75 mg/m²), administered every three weeks for 4 cycles;
- (V) Docetaxel combined with epirubicin and cyclophosphamide (T: 75 mg/m², E: 90 mg/m², C: 500 mg/m²), administered every three weeks for 6 cycles.

Additionally, various other chemotherapy regimens were available. For patients exhibiting HER2 overexpression, targeted therapy with trastuzumab or pertuzumab was recommended for a period of 1 year.

Statistical analysis

The statistical analyses were conducted using Statistical Product and Service Solutions (SPSS) software, version 25.0. Data conforming to a normal distribution were expressed as the mean ± standard deviation, while data not conforming to a normal distribution were reported as the median (interquartile range). For data consistent with a normal distribution, an independent samples *t*-test was used for comparisons between two groups, while a one-way analysis of variance (ANOVA) was used for comparisons among multiple groups. For data that did not conform to a normal distribution, the Mann-Whitney *U* test was used for comparisons between two groups, while the Kruskal-Wallis (*H*) test was used for comparisons among multiple groups. A two-sided test with a significance level of P<0.05 was considered statistically significant.

The paired sample *t*-test was employed to compare blood lipid levels and BMI before and after chemotherapy within the observational group, control group, chemotherapy drug group, and the targeted therapy combination subgroup. The alterations in blood lipid levels and BMI were quantified across the observational group, control group, and three chemotherapy subgroups. The differences were calculated by subtracting the pre-chemotherapy values from the post-chemotherapy values. A one-way ANOVA was employed to evaluate the significance of the differences in the degree of change in the BMI and lipid levels among the observational group, the control group, and the three chemotherapy drug subgroups.

Ethics

This retrospective analysis was approved by the Ethics

Committee of Zhejiang Provincial Hospital of Traditional Chinese Medicine (No. 2023-KLS-036-01) and conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013). The individual consent for this retrospective analysis was waived.

Results

Patient characteristics

In this study, a cohort of 180 eligible breast cancer patients was identified (Figure 1). Based on the administration of SLBZP during chemotherapy, the patients were categorized into the following two groups: the observational group, which received SLBZP (N=131), and the control group, which did not receive SLBZP (N=49). Table 1 sets out the demographic and clinical characteristics of the patients. The mean age of the 180 patients was 50.76 years. The demographic and clinical characteristics of the study population revealed no significant differences between the two groups in terms of age, menopausal status, smoking habits, excessive alcohol consumption, tumor location, molecular typing, chemotherapy regimen, and targeted therapy (P>0.05). However, a significant difference was observed between the two groups in terms of TNM staging (P<0.05).

Effects of chemotherapy on blood lipid levels and BMI

In this study, no significant differences in BMI and blood lipid levels were observed between the observational group and the control group before chemotherapy (P>0.05). After chemotherapy, the control group showed a significant increase in apolipoprotein A1 (ApoA1) level compared to the observational group (t=-2.5851, P=0.02), while BMI and other blood lipid parameters remained similar between the groups (P>0.05).

Table 2 presents the effects of chemotherapy on blood lipid levels and BMI in both the observational and control groups. In the observational group, BMI increased significantly after chemotherapy (P=0.02), whereas HDL-C (P=0.001) and ApoA1 (P<0.001) levels decreased significantly. TC, TG, and LDL-C levels remained unchanged (P>0.05). In the control group, the post-chemotherapy levels of TC (P=0.03), TG (P=0.001), LDL-C (P=0.02), and apolipoprotein B (ApoB) (P=0.01) significantly increased compared to the pre-chemotherapy levels, while BMI, HDL-C and ApoA1 levels remained unchanged (P>0.05).

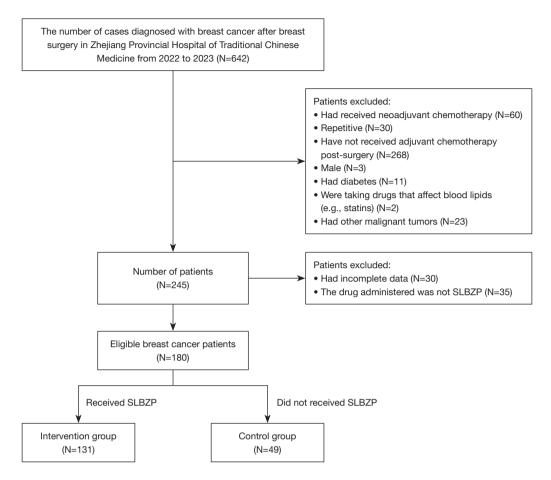


Figure 1 Flow chart of patient selection and exclusion. SLBZP, Shenling Baizhu Powder.

To assess the effects of various chemotherapy agents on lipid profiles and BMI, patients in both the control and observational groups were categorized into the following three subgroups: the taxane subgroup; the taxane followed by anthracycline subgroup; and the anthracycline subgroup. The results of the subgroup analysis are set out in *Table 2*. Within the observational group, no statistically significant differences in BMI and blood lipid levels were observed among the three subgroups before and after chemotherapy (P>0.05). A significant difference in TG levels before chemotherapy was observed among the three subgroups within the control group (F=3.646, P=0.03). Specifically, the TG levels of the taxane subgroup were higher than those of the anthracycline subgroup before chemotherapy (P=0.03). No significant differences were found in other pre-chemotherapy indicators, BMI, or blood lipid levels post-chemotherapy (P>0.05). When comparing each chemotherapy drug subgroup between the control and observational groups, no significant differences were

detected in BMI or blood lipid levels (P>0.05).

In the observational group, the taxane followed by anthracycline subgroup showed a significant BMI increase (P=0.007) and decreases in HDL-C (P=0.007) and ApoA1 (P<0.001) following chemotherapy. The taxane subgroup also had significantly lower HDL-C levels post-chemotherapy (P=0.003). No significant changes were observed in TC, TG, LDL-C, and ApoB levels across the three subgroups (P>0.05). In the control group, the taxane followed by anthracycline subgroup showed significant increases in TG (P=0.002) and LDL-C (P=0.02) levels post-chemotherapy. No significant changes in BMI or other lipid indices were found in the other chemotherapy drug subgroups (P>0.05).

Effects of targeted therapy on lipid levels and BMI

For patients exhibiting HER2 overexpression, chemotherapy was frequently administered in conjunction

Table 1 Demographic and clinical characteristics of the study cohort

Variable	Overall (N=180)	G		
		Control group [N=49 (27%)]	Shenling Baizhu Powder [N=131 (73%)]	P value [#]
Age (years)	50.76±9.89 50.04±8.56		51.02±10.36	0.52
Menopause				0.65
No	96 (53.33)	28 (57.14)	68 (51.91)	
Yes	84 (46.67)	21 (42.86)	63 (48.09)	
Smoking				-
No	180 (100.00)	49 (100.00)	131 (100.00)	
Excessive alcohol intake				-
No	180 (100.00)	49 (100.00)	131 (100.00)	
Tumor location				0.16
Left	93 (51.67)	30 (61.22)	63 (48.09)	
Right	87 (48.33)	19 (38.78)	68 (51.91)	
Molecular subtyping				0.82
HER2 overexpression	38 (21.11)	11 (22.45)	27 (20.61)	
Luminal A	57 (31.67)	13 (26.53)	44 (33.59)	
Luminal B	53 (29.44)	15 (30.61)	38 (29.01)	
TNBC	32 (17.78)	10 (20.41)	22 (16.79)	
TNM staging				0.01**
1	96 (53.33)	34 (69.39)	62 (47.33)	
II	68 (37.78)	10 (20.41)	58 (44.27)	
III	16 (8.89)	5 (10.20)	11 (8.40)	
Adjuvant chemotherapy regimen				0.83
Anthracycline and taxane	87 (48.33)	22 (44.90)	65 (49.62)	
Anthracycline	16 (8.89)	5 (10.20)	11 (8.40)	
Taxane	77 (42.78)	22 (44.90)	55 (41.98)	
Targeted therapy				0.75
No	119 (66.11)	31 (63.27)	88 (67.18)	
Yes	61 (33.89)	18 (36.73)	43 (32.82)	

Data are presented as mean \pm standard deviation or n (%). *, Welch two-sample *t*-test; Pearson's Chi-squared test. **, P \le 0.01; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; TNM, tumor node metastasis.

with targeted therapy. Given that targeted therapy was commonly combined with taxane chemotherapy, we further stratified the taxane subgroup and the taxane followed by anthracycline subgroup based on the presence or absence of targeted therapy (*Table 3*). In the observational group,

patients treated with taxane followed by anthracycline without targeted therapy showed a significant BMI increase (P=0.01) post-treatment. Those receiving targeted therapy experienced significant decreases in TC (P=0.02) and HDL-C (P=0.047) levels. ApoA1 levels significantly

Table 2 A comparative analysis of lipid levels and BMI pre- and post-chemotherapy

*	Shenling Baizhu Powder			Control group			
Parameters	Before chemotherapy	After chemotherapy	Р	Before chemotherapy	After chemotherapy	Р	
Entire group		N=131			N=49		
BMI (kg/m²)	23.2 (21.3, 24.8)	23.4 (21.4, 25.1)	0.02*	22.7 (21.3, 24.9)	22.9 (21.4, 25.6)	0.10	
TC (mmol/L)	5.09±0.89	4.96±0.91	0.09	4.84±0.86	5.10±0.92	0.03*	
TG (mmol/L)	1.48 (1.07, 2.19)	1.66 (1.19, 2.22)	0.34	1.27 (0.88, 2.01)	1.73 (1.14, 2.17)	0.001***	
LDL-C (mmol/L)	2.73 (2.30, 3.20)	2.71 (2.23, 3.20)	0.62	2.70±0.77	2.86±0.73	0.02*	
HDL-C (mmol/L)	1.34 (1.16, 1.50)	1.25 (1.07, 1.46)	0.001***	1.33±0.36	1.35±0.34	0.68	
ApoA1 (g/L)	1.41 (1.27, 1.53)	1.33 (1.21, 1.47)	<0.001***	1.38±0.20	1.44±0.25	0.06	
ApoB (g/L)	0.98 (0.86, 1.11)	0.99 (0.88, 1.13)	0.13	0.93±0.20	0.98±0.20	0.01**	
Taxane		N=55			N=22		
BMI (kg/m²)	23.1 (21.5, 25.0)	23.4 (21.2, 25.0)	0.36	22.6 (21.2, 24.2)	23.1 (21.5, 24.8)	0.09	
TC (mmol/L)	5.10±0.97	4.94±0.85	0.13	4.89±0.95	5.12±0.91	0.16	
TG (mmol/L)	1.47 (1.07, 2.19)	1.57 (1.21, 2.31)	0.18	1.55±0.62	1.71±0.63	0.38	
LDL-C (mmol/L)	2.78±0.80	2.73±0.69	0.50	2.32 (2.07, 2.96)	2.71 (2.15, 3.33)	0.07	
HDL-C (mmol/L)	1.37±0.30	1.25±0.26	0.003**	1.44±0.34	1.45±0.33	0.84	
ApoA1 (g/L)	1.40±0.18	1.34±0.20	0.09	1.43±0.16	1.50±0.27	0.11	
ApoB (g/L)	0.99±0.21	1.01±0.19	0.34	0.93±0.21	0.99±0.21	0.07	
Anthracycline and taxane		N=65			N=22		
BMI (kg/m²)	23.2 (21.2, 24.6)	23.4 (21.6, 25.3)	0.007**	22.9 (22.0, 25.9)	22.9 (21.6, 26.3)	0.81	
TC (mmol/L)	5.12±0.78	5.01±0.92	0.30	4.73±0.86	5.03±1.01	0.14	
TG (mmol/L)	1.82±1.21	1.80±0.86	0.90	1.46±0.62	1.92±0.88	0.002**	
LDL-C (mmol/L)	2.75 (2.42, 3.19)	2.73 (2.28, 3.08)	0.92	2.60 (1.96, 3.22)	3.14 (2.31, 3.33)	0.02*	
HDL-C (mmol/L)	1.34 (1.18, 1.50)	1.25 (1.06, 1.48)	0.007**	1.23±0.35	1.24±0.35	0.86	
ApoA1 (g/L)	1.43 (1.30, 1.54)	1.33 (1.23, 1.46)	<0.001***	1.34±0.23	1.36±0.22	0.66	
ApoB (g/L)	0.98 (0.87, 1.08)	0.99 (0.88, 1.11)	0.27	0.93±0.22	0.98±0.20	0.08	
Anthracycline		N=11			N=5		
BMI (kg/m²)	23.3±3.1	22.9±3.5	0.18	20.5 (20.2, 23.7)	21.2 (20.6, 25.7)	0.27	
TC (mmol/L)	4.89±1.08	4.82±1.18	0.86	5.06±0.42	5.29±0.63	0.55	
TG (mmol/L)	1.69±1.15	1.69±1.25	>0.99	0.76±0.15	1.18±0.57	0.19	
LDL-C (mmol/L)	2.72±0.76	2.59±0.73	0.56	3.07 (2.72, 4.10)	2.98 (2.75, 3.74)	0.89	
HDL-C (mmol/L)	1.31±0.34	1.41±0.45	0.40	1.32±0.43	1.38±0.27	0.68	
ApoA1 (g/L)	1.38±0.24	1.31±0.22	0.48	1.33±0.15	1.47±0.25	0.07	
ApoB (g/L)	1.00±0.22	1.03±0.26	0.75	0.96±0.13	0.98±0.11	0.77	

Data are presented as mean \pm standard deviation or M (P_{25} , P_{75}). *, $P \le 0.05$; **, $P \le 0.01$; ***, $P \le 0.001$. ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

Table 3 A stratified analysis based on targeted therapy comparing blood lipid levels and BMI before and after chemotherapy

		Shenling Baizhu Powder			Control group		
Subgroups	bgroups Parameters		After chemotherapy	Р	Before chemotherapy	After chemotherapy	Р
Taxane							
Have targeted			N=18		N=12		
therapy	BMI (kg/m²)	22.4 (20.9, 23.6)	22.8 (21.0, 24.7)	0.60	21.3 (19.6, 23.6)	21.7 (19.7, 23.4)	0.20
	TC (mmol/L)	5.30±0.75	5.06±0.75	0.17	5.11±1.06	5.36±0.95	0.33
	TG (mmol/L)	1.74 (1.31, 2.30)	1.97 (1.17, 2.44)	0.65	1.47±0.60	1.75±0.76	0.30
	LDL-C (mmol/L)	2.83±0.51	2.71±0.57	0.32	2.70 (2.17, 3.09)	2.92 (2.44, 3.52)	0.0
	HDL-C (mmol/L)	1.41±0.31	1.27±0.31	0.04*	1.49±0.39	1.44±0.28	0.6
	ApoA1	1.41±0.21	1.31±0.22	0.03*	1.41±0.17	1.47±0.26	0.3
	АроВ	1.07±0.17	1.06±0.17	0.85	0.96±0.23	1.04±0.22	0.1
No targeted therapy			N=37			N=10	
	BMI (kg/m²)	23.5±3.0	23.6±2.8	0.45	22.8 (22.3, 25.6)	23.6 (22.9, 26.2)	0.2
	TC (mmol/L)	5.01±1.06	4.90±0.89	0.38	4.64±0.75	4.84±0.83	0.3
	TG (mmol/L)	1.62±0.92	1.74±0.66	0.35	1.64±0.66	1.65±0.46	0.9
	LDL-C (mmol/L)	2.76±0.92	2.74±0.75	0.84	2.19 (2.00, 2.57)	2.24 (1.93, 3.17)	0.7
	HDL-C (mmol/L)	1.35±0.30	1.23±0.24	0.03*	1.38±0.28	1.45±0.39	0.3
	ApoA1 (g/L)	1.39±0.17	1.36±0.20	0.52	1.46±0.17	1.55±0.29	0.2
	ApoB (g/L)	0.96±0.23	1.00±0.20	0.21	0.89±0.18	0.92±0.20	0.4
Anthracycline and	d taxane						
Have targeted			N=25			N=14	
therapy	BMI (kg/m²)	23.2 (20.8, 25.3)	23.7 (20.7, 27.2)	0.29	23.0 (22.6, 27.3)	22.9 (22.2, 28.0)	0.9
	TC (mmol/L)	5.06±0.85	4.67±0.80	0.02*	4.75±0.88	5.31±1.06	0.02
	TG (mmol/L)	1.49 (1.01, 2.14)	1.51 (1.20, 1.87)	0.52	1.39±0.63	1.88±0.92	0.02
	LDL-C (mmol/L)	2.77±0.54	2.58±0.58	0.20	2.60 (1.96, 3.34)	3.07 (2.23, 3.40)	0.1
	HDL-C (mmol/L)	1.36 (1.16, 1.59)	1.22 (0.97, 1.45)	0.047*	1.23±0.32	1.32±0.33	0.2
	ApoA1 (g/L)	1.43 (1.25, 1.54)	1.33 (1.22, 1.41)	0.02*	1.34±0.22	1.44±0.22	0.1
	ApoB (g/L)	0.98(0.89, 1.09)	0.91 (0.87, 1.04)	0.16	0.93±0.24	1.01±0.21	0.02
No targeted	N=40 N=8						
therapy	BMI (kg/m²)	22.8±2.1	23.4±2.4	0.01**	22.5 (21.0, 25.1)	22.8 (21.5, 24.1)	0.7
	TC (mmol/L)	5.16±0.74	5.22±0.93	0.63	4.71±0.88	4.54±0.73	0.6
	TG (mmol/L)	1.80±1.05	1.89±0.89	0.59	1.59±0.63	2.00±0.86	0.0
	LDL-C (mmol/L)	2.69 (2.41, 3.29)	2.85 (2.37, 3.27)	0.29	2.68 (1.93, 3.22)	3.18 (2.37, 3.29)	0.0
	HDL-C (mmol/L)	1.34 (1.19, 1.49)	1.26(1.10, 1.48)	0.07	1.22±0.43	1.09±0.34	0.1
	ApoA1 (g/L)	1.42±0.16	1.33±0.20	0.004**	1.34±0.27	1.24±0.17	0.1
	ApoB (g/L)	0.98 (0.86, 1.07)	1.02 (0.92, 1.16)	0.07	0.92±0.19	0.93±0.20	0.9

Data are presented as mean \pm standard deviation or M (P_{25} , P_{75}). *, $P \le 0.05$; **, $P \le 0.01$. ApoA1, apolipoprotein A1; ApoB, apolipoprotein B; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

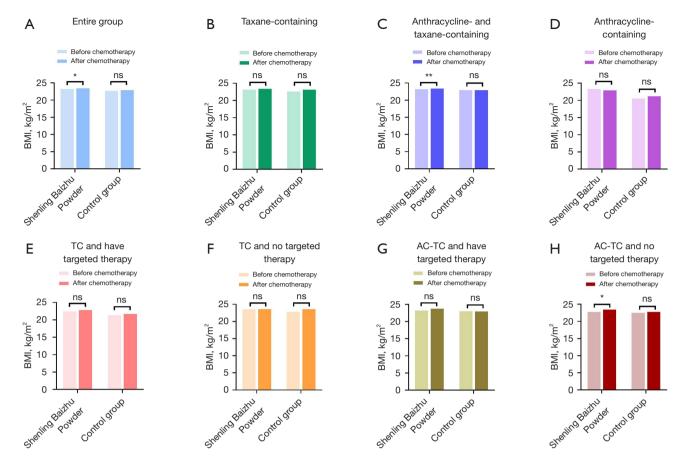


Figure 2 Variations in BMI pre- and post-chemotherapy across distinct cohorts. (A) Changes in BMI before and after chemotherapy in both the observational and control groups. (B-D) Effects of different chemotherapy regimens on BMI in both the observational and control groups. (E-H) Effects of targeted therapy on BMI in both the observational and control groups. *, P≤0.05; **, P≤0.01; ns, P>0.05. AC, anthracycline; BMI, body mass index; TC, taxane.

decreased regardless of targeted therapy (P=0.004, P=0.02). In the taxane subgroup, HDL-C levels dropped significantly in both therapy groups compared to pre-chemotherapy levels (P=0.03, P=0.04), and ApoA1 levels decreased significantly in the targeted therapy group (P=0.03). No significant changes were noted in TG, LDL-C, and ApoB levels (P>0.05).

In the control group, the taxane followed by anthracyclines subgroup showed significantly increased post-chemotherapy levels of TC, TG, and ApoB (P=0.02) in the non-targeted therapy cohort. However, there were no significant changes in BMI, LDL-C, HDL-C, and ApoA1 levels (P>0.05).

The variations in BMI, and the TC, TG, HDL-C, LDL-C, ApoA1, and ApoB levels between the observational and control groups across different subgroups, both before and after chemotherapy, were depicted in *Figures 2-8*.

Comparison of the magnitude of lipid alterations after chemotherapy

Further analyses were conducted to investigate the extent of changes in the lipid levels and BMI between the control group and the observational group, as well as among the chemotherapy agent subgroups. In the observational group, the degree of change in BMI was statistically significant across the three subgroups (H=6.667, P=0.04), with the taxane followed by anthracycline subgroup exhibiting a significantly greater change in BMI compared to the anthracycline subgroup (P=0.045). However, the extent of changes in TC (F=0.075, P=0.93), TG (H=0.586, P=0.75), LDL-C (H=0.919, P=0.63), HDL-C (H=5.846, P=0.054), ApoA1 (H=0.546, P=0.76), and ApoB (H=0.057, P=0.97) did not differ significantly among the three subgroups. In

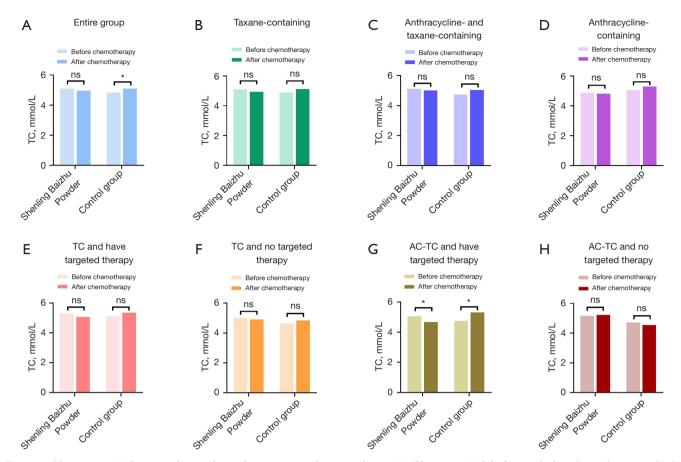


Figure 3 Variations in TC pre- and post-chemotherapy across distinct cohorts. (A) Changes in TC before and after chemotherapy in both the observational and control groups. (B-D) Effects of different chemotherapy regimens on TC in both the observational and control groups. (E-H) Effects of targeted therapy on TC in both the observational and control groups. *, $P \le 0.05$; ns, P > 0.05. AC, anthracycline; TC, taxane.

the control group, no significant differences were observed in the changes of the blood lipid levels and BMI before and after chemotherapy among the three subgroups (P>0.05). Conversely, the observational group exhibited significant differences in the changes of the ApoA1 levels before and after chemotherapy compared to the control group (H=15.681, P=0.008). The changes in ApoA1 levels in the taxane and the taxane-plus-anthracycline subgroups of the control group were significantly greater than those in the observational group.

Discussion

This study is the first to investigate the effects of SLBZP on blood lipid levels and BMI in breast cancer patients undergoing adjuvant chemotherapy. We found that the levels of TC, TG, LDL-C, and ApoB in the control

group were significantly elevated post-chemotherapy compared to pre-chemotherapy, a result that aligned with the existing literature (5,20). In the observational group that received SLBZP, no significant alterations were observed in the TC, TG, and LDL-C levels pre- and postchemotherapy. However, the HDL-C and ApoA1 levels decreased significantly, and BMI increased significantly post-chemotherapy compared to pre-chemotherapy. Adjuvant chemotherapy has the potential to induce longterm metabolic disorders in patients, leading to conditions such as dyslipidemia and diabetes (21). Elevated LDL-C, in particular, is recognized as a critical risk factor for cardiovascular disease. As the survival rates of breast cancer patients increased, cardiovascular disease has emerged as the predominant cause of mortality in this population (22). Consequently, LDL-C has become a primary target in the management of dyslipidemia (23,24). The present study

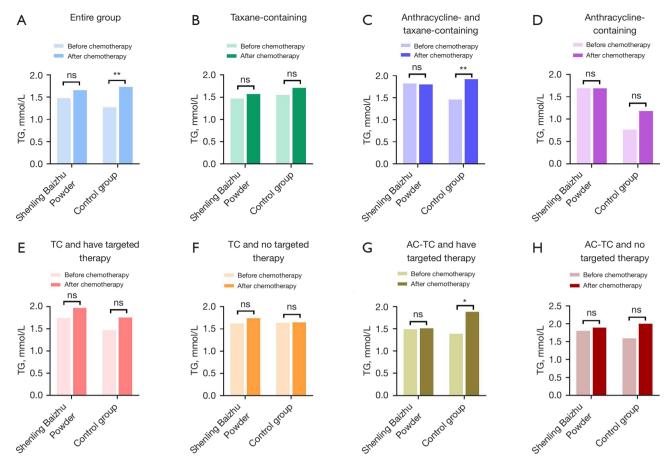


Figure 4 Variations in TG pre- and post-chemotherapy across distinct cohorts. (A) Changes in TG before and after chemotherapy in both the observational and control groups. (B-D) Effects of different chemotherapy regimens on TG in both the observational and control groups. (E-H) Effects of targeted therapy on TG in both the observational and control groups. *, $P \le 0.05$; **, $P \le 0.01$; ns, P > 0.05. AC, anthracycline; TC, taxane; TG, triglyceride.

showed that SLBZP effectively mitigated chemotherapy-induced dyslipidemia in breast cancer patients by reducing elevated TC, TG, and LDL-C levels. This finding suggests that SLBZP could serve as a preventive strategy to minimize the adverse effects of chemotherapy on lipid profiles. In clinical practice, SLBZP could be considered as an adjunctive therapy for patients undergoing chemotherapy, particularly those at high risk for dyslipidemia. By reducing LDL-C levels, SLBZP may contribute to the primary prevention of cardiovascular disease in this population.

Chemotherapy, a prevalent modality for cancer treatment, frequently induces gastrointestinal toxicity across various regimens, which manifests clinically as nausea, vomiting, abdominal pain, diarrhea, and weight loss (25). According to TCM theory, the pathogenesis of obesity is impaired spleen function, resulting in the accumulation

of phlegm in the body. This phlegm subsequently leads to blood stasis, creating a cyclical relationship where blood stasis further exacerbates phlegm accumulation, ultimately causing obstruction by both phlegm and blood stasis (26). The pathogenesis of dyslipidemia includes spleen deficiency, impaired movement and metabolism, insufficiency of clear qi, and the accumulation of turbid Yin, which collectively contributed to the generation of dampness and phlegm. This phlegm dampness further obstructed gi movement, disrupted the transportation functions of the spleen and stomach, exacerbated spleen deficiency, and aggravated lipid turbidity (27). Additionally, chemotherapy drugs, which are highly toxic substances, primarily inflict damage on the spleen and stomach (28). During chemotherapy, the spleen and stomach often exhibit weakened function and abnormal motility, leading to the production of phlegm

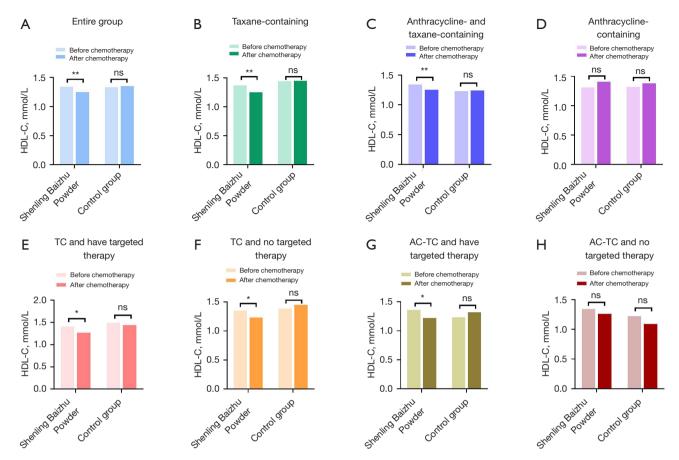


Figure 5 Variations in HDL-C pre- and post-chemotherapy across distinct cohorts. (A) Changes in HDL-C before and after chemotherapy in both the observational and control groups. (B-D) Effects of different chemotherapy regimens on HDL-C in both the observational and control groups. (E-H) Effects of targeted therapy on HDL-C in both the observational and control groups. *, P≤0.05; **, P≤0.01; ns, P>0.05. AC, anthracycline; HDL-C, high-density lipoprotein cholesterol; TC, taxane.

dampness within the body. This condition frequently manifested in symptoms such as loss of appetite, nausea, vomiting, dyslipidemia, overweight, and obesity. Research indicates that SLBZP may enhance digestive function, alter the composition and dysfunction of the intestinal microbial community (29), and ameliorate metabolic disorders by modulating metabolic pathways, including those involved in energy metabolism, amino acid metabolism, intestinal microbiota, and host co-metabolism (30). In this study, the BMI of the observational group was significantly higher post-chemotherapy than pre-chemotherapy, while the control group exhibited no significant change. This outcome may be attributed to the administration of SLBZP, which was known to enhance digestive function, alleviate gastrointestinal adverse reactions associated with chemotherapy, and subsequently increase patient appetite, thereby contributing to weight gain post-chemotherapy.

In addition, the baseline body composition of the observational group may have differed from that of the control group. Patients with lower baseline muscle mass or higher baseline body fat may be more prone to weight gain during chemotherapy. In summary, the observed increase in BMI in the SLBZP group can be attributed to a combination of factors, including the alleviation of gastrointestinal symptoms by SLBZP and differences in baseline body composition. Further studies are needed to elucidate the specific contributions of these factors. This finding highlights the need for careful monitoring of weight changes in patients receiving SLBZP.

This study found that various chemotherapy drugs exerted distinct effects on blood lipid levels and BMI. Specifically, it was observed that the administration of taxane and anthracycline-based drugs, as well as taxane-based regimens, can significantly induce dyslipidemia (5,31).

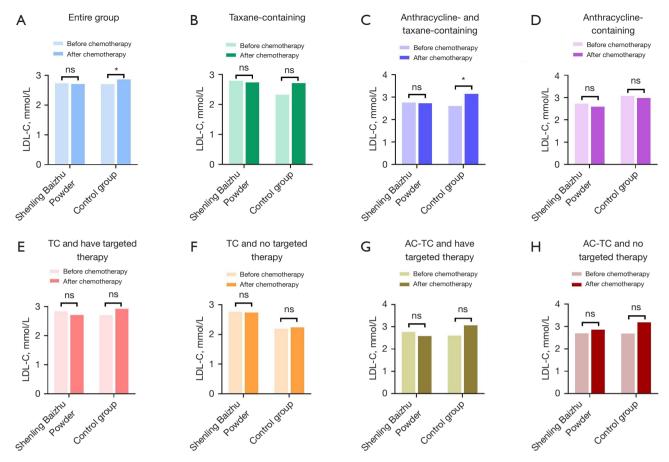


Figure 6 Variations in LDL-C pre- and post-chemotherapy across distinct cohorts. (A) Changes in LDL-C before and after chemotherapy in both the observation and control groups. (B-D) Effects of different chemotherapy regimens on LDL-C in both the observational and control groups. (E-H) Effects of targeted therapy on LDL-C in both the observational and control groups. *, $P \le 0.05$; ns, P > 0.05. AC, anthracycline; LDL-C, low-density lipoprotein cholesterol; TC, taxane.

Conversely, chemotherapy based solely on anthracyclinebased drugs did not have a significant effect on blood lipid levels (32). In this study, in the control group, the TG and LDL-C levels of the taxane followed by anthracycline subgroup were significantly elevated post-chemotherapy compared to pre-chemotherapy. In the observational group, the BMI of the taxane followed by anthracycline subgroup was significantly higher, while the HDL-C and ApoA1 levels were significantly lower. Additionally, the HDL-C levels of the taxane subgroup were significantly reduced following chemotherapy. Conversely, no significant changes were observed in BMI and blood lipid levels within the anthracycline-based drug subgroups, which was consistent with existing reports. This suggests that the choice of chemotherapy regimen should be carefully considered, especially in patients with pre-existing dyslipidemia or at

high risk for cardiovascular complications.

Notably, breast cancer patients with HER2 overexpression often receive targeted therapy in conjunction with chemotherapy. However, few studies have investigated the effects of targeted therapy on blood lipid levels in such patients. One study reported that the cholesterol content of the cell membrane was positively correlated with the distribution of HER2 on the cell surface (33). The proposed mechanism suggested that cholesterol increased the rigidity of the cell membrane and reduced its fluidity. Consequently, lower cholesterol levels facilitated the internalization and degradation of HER2. This interaction may have implications for blood lipid levels, and thus warrants further investigation.

The mechanisms by which chemotherapy induced dyslipidemia are complex and multifactorial. First,

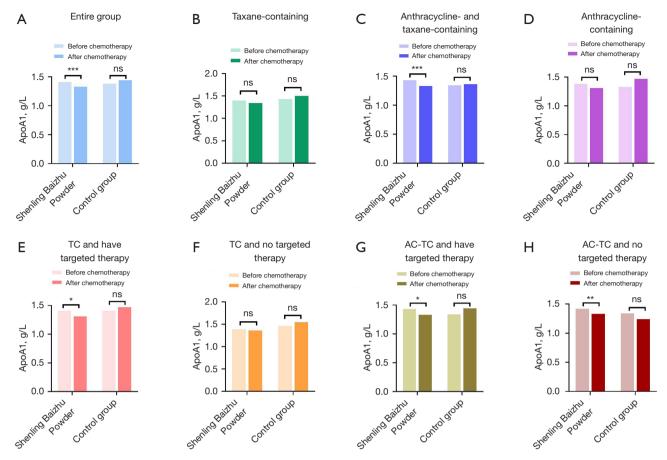


Figure 7 Variations in ApoA1 pre- and post-chemotherapy across distinct cohorts. (A) Changes in ApoA1 before and after chemotherapy in both the observation and control groups. (B-D) Effects of different chemotherapy regimens on ApoA1 in both the observational and control groups. (E-H) Effects of targeted therapy on ApoA1 in both the observational and control groups. *, $P \le 0.05$; **, $P \le 0.01$; ***, $P \le 0.001$; ns, P > 0.05. AC, anthracycline; ApoA1, apolipoprotein A1; TC, taxane.

certain chemotherapeutic agents can disrupt normal lipid metabolism pathways. For instance, paclitaxel has been reported to inhibit the cellular uptake of cholesterol and enhance the degradation of HDL-C, thereby reducing HDL-C levels. Second, chemotherapy can impair endothelial cell function, which in turn affects the balance of vasodilatory and vasoconstrictive factors, subsequently influencing lipid levels. Endothelial cellsecreted factors, such as nitric oxide and endothelin-1, can serve as indirect indicators of endothelial function. Furthermore, chemotherapy has the potential to elicit a systemic inflammatory response, subsequently modifying cytokine levels, which played a role in the regulation of lipid metabolism. Specifically, inflammatory mediators such as tumor necrosis factor-alpha and interleukin-6 have been implicated in influencing lipid metabolic processes. This

retrospective study showed that SLBZP could mitigate the adverse effects of chemotherapy-induced dyslipidemia. The plants used in SLBZP contain a variety of phytochemicals that contribute to the reduction of lipid levels and the improvement of overall health. These phytochemicals work synergistically to balance the body's functions and potentially prevent the development of various diseases. For instance, Pseudostellaria heterophylla contains polysaccharides and heterophyllin B, which have immunomodulatory and antiinflammatory effects that can help reduce lipid accumulation and improve lipid profiles. Poria cocos is rich in triterpenic acids and polysaccharides that have anti-inflammatory and antioxidant properties, helping to reduce lipid accumulation in the liver and improve lipid profiles by modulating the expression of enzymes involved in lipid metabolism. Atractylodes macrocephala contains sesquiterpenes that

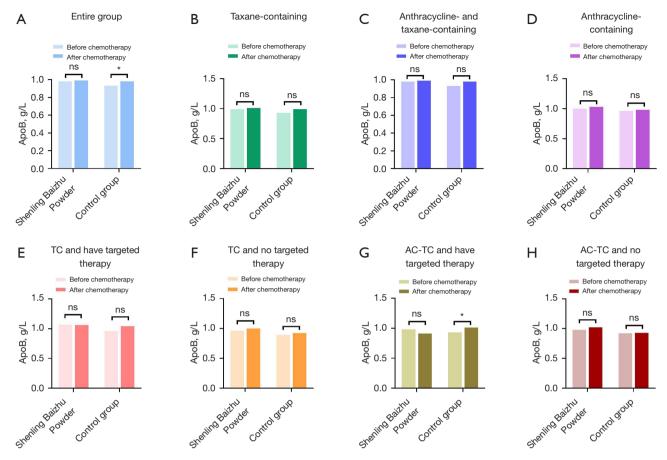


Figure 8 Variations in ApoB pre- and post-chemotherapy across distinct cohorts. (A) Changes in ApoB before and after chemotherapy in both the observational and control groups. (B-D) Effects of different chemotherapy regimens on ApoB in both the observational and control groups. (E-H) Effects of targeted therapy on ApoB in both the observational and control groups. *, P≤0.05; ns, P>0.05. AC, anthracycline; ApoB, apolipoprotein B; TC, taxane.

enhance gastrointestinal function, reduce water retention, and exhibit anti-inflammatory effects, which can help mitigate the inflammatory processes associated with dyslipidemia. Dioscorea opposita has polysaccharides and steroidal saponins that have immunomodulatory and antiinflammatory effects, contributing to the reduction of lipid accumulation and improvement of lipid profiles. Lablab purpureus contains flavonoids and saponins that have anti-inflammatory and antioxidant properties, which can help reduce lipid accumulation and improve lipid profiles. Nelumbo nucifera contains alkaloids like neferine, which have anti-inflammatory and antioxidant effects that can help reduce lipid accumulation and improve lipid profiles. Coix lacryma-jobi contains polysaccharides and triterpenoids that have anti-inflammatory and antioxidant properties, contributing to the reduction of lipid accumulation and

improvement of lipid profiles. Amonum villosum contains essential oils and flavonoids that have anti-inflammatory and antioxidant properties, which can help reduce lipid accumulation and improve lipid profiles. Platycodon grandiflorum contains saponins that have anti-inflammatory and antioxidant properties and can help reduce lipid accumulation and improve lipid profiles by modulating the expression of genes involved in lipid metabolism. Glycyrrhiza uralensis contains glycyrrhizin and flavonoids that have anti-inflammatory and antioxidant properties, which can help reduce lipid accumulation and improve lipid profiles. These components work together to modulate the immune system, reduce inflammation and oxidative stress, regulate lipid metabolism, and improve overall metabolic health. Further experiments can be conducted to investigate the impact of SLBZP on lipid metabolism, endothelial dysfunction, and cytokine alterations induced by chemotherapy, and to explore the mechanisms by which SLBZP mitigated the side effects associated with chemotherapy-induced dyslipidemia. And we intend to isolate pure extracts from the plants used in SLBZP to better understand their individual contributions to lipid reduction and overall health benefits. This approach will allow us to develop more targeted and effective formulations. Additionally, we are considering the creation of additional products that leverage the synergistic effects of these phytochemicals to address specific health conditions, such as dyslipidemia and metabolic disorders. We believe that by isolating and characterizing the active components, we can optimize the therapeutic efficacy of SLBZP and potentially develop novel interventions for metabolic health.

To the best of our knowledge, this was the first study to examine the effects of SLBZP on blood lipid levels and BMI in breast cancer patients undergoing chemotherapy, and to assess the effects of targeted therapy on these parameters. This is important since Asia had experienced a surge in breast cancer cases (34) and TCM is more commonly used in Asia.

However, this study had some limitations, including its retrospective design, and its inability to fully exclude some confounding factors. Furthermore, the data were collected from a single center. To further validate our findings and enhance the robustness of the conclusions, larger, prospective studies are warranted. Such studies would allow for more rigorous control over variables and a more comprehensive assessment of the long-term effects of SLBZP on patient outcomes. Prospective studies can provide a clearer understanding of the causal relationships between SLBZP use and the observed outcomes by ensuring that data collection is systematic and standardized from the outset. This approach would also enable the inclusion of a broader and more diverse patient population, thereby increasing the generalizability of the findings.

Conclusions

Chemotherapy has been observed to induce dyslipidemia, which was characterized by significant increases in TC, TG, LDL-C, and ApoB levels, in breast cancer patients. SLBZP effectively mitigated chemotherapy-induced dyslipidemia, as indicated by stable TC, TG, and LDL-C levels post-chemotherapy. However, the oral administration of SLBZP was associated with an increase in BMI among patients following chemotherapy, which might be

attributed to its ability to alleviate chemotherapy-induced gastrointestinal adverse effects. Taxane-based chemotherapy drugs had greater adverse effects on blood lipid levels and BMI, whereas anthracycline-based drugs had minimal impact. Based on the findings from our study and the existing literature, we recommend that breast cancer patients receiving adjuvant chemotherapy consider oral administration of SLBZP, particularly those undergoing taxane-based chemotherapy regimens. In summary, while our study offers a promising direction for future research, the need for larger, prospective studies cannot be overstated. These studies will be crucial in confirming the therapeutic potential of SLBZP and guiding clinical practice in the management of breast cancer patients undergoing chemotherapy.

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None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr. amegroups.com/article/view/10.21037/tcr-2024-2658/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-2024-2658/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki

(as revised in 2013). The study was approved by the Ethics Committee of the Zhejiang Provincial Hospital of Traditional Chinese Medicine (No. 2023-KLS-036-01) and individual consent for this retrospective analysis was waived.

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