ORIGINAL ARTICLE

WEIGHT CHANGES IN PATIENTS WITH HODGKIN LYMPHOMA FOLLOWING TREATMENT: EXPERIENCE FROM A CANCER HOSPITAL

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Background: Some recent studies have suggested that patients with Hodgkin lymphoma who undergo remission following treatment are likely to experience significant weight gain and may become overweight or obese. The association between treatment for Hodgkin lymphoma and subsequent weight gain has not been explored in Pakistan. We undertook a review of weight changes in adult Hodgkin lymphoma patients who received treatment at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore. **Methods:** In this longitudinal study, we collected and analysed secondary data including adult patients who received treatment for Hodgkin lymphoma at our institute from January 2010 till December 2013. We retrospectively noted baseline demographic, clinical characteristics, details about treatment received and change in weight from baseline at start of treatment to 6, 12, and 18 months after start of treatment. **Results:** A total of 470 patients registered for Hodgkin lymphoma at our centre. Data were available for 402 patients who were included in this study. Progressive increase in weight was observed in patients after treatment. The mean weight gain from the start of treatment to 6, 12, and 18 months was 3.1 kg, 7.1 kg, and 9.5 kg, respectively. Weight gain was not significantly associated with age or sex of patients. Weight gain was significantly associated with higher stages of cancer, response to treatment and B symptoms. **Conclusion:** The evaluation of Hodgkin lymphoma patients after treatment demonstrated considerable tendency for weight gain. Further work is warranted to explore this association and its impact on HL survivors.

Keywords: Weight gain; Hodgkin Lymphoma; Survivors

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INTRODUCTION

Hodgkin lymphoma (HL) is one of the most curable cancers worldwide.[1] Depending on the stage and risk factors of disease, five years' survival of Hodgkin's lymphoma is now more than 80% with current cancer therapies.[2] Treatment with chemotherapy, radiotherapy or both is based on initial evaluation and the stage of the disease. During and after treatment, patients are regularly evaluated for treatment response and disease relapse. However, successful treatment is associated with long term side effects. HL survivors may present years after treatment with therapy related complications like secondary cancers, cardiovascular disease, lung disease and hypothyroidism.[3,4] Regular screening is therefore advised, as an early detection of these complications may lead to better management. Few studies have explored the association between cancer survivors and weight gain or obesity.[5]

Obesity is a chronic health problem distributed all over the world and is associated with increased risk of cardiovascular disease, diabetes mellitus, cerebrovascular accident and may lead to increased morbidity and mortality.[6,7] Obesity can affect already compromised chronic health conditions of HL patients. Childhood survivors of acute lymphoblastic leukaemia have shown a significant weight gain after treatment.[8] One study of Acute Lymphoblastic Leukaemia (ALL) survivors revealed that 28% of patients were overweight and 17% were obese as compared to their siblings.[9] Increased incidence of HL in obese persons has been highlighted.[10] However, an increase in body mass index as a result of lymphoma treatment has not been studied on a large scale. In one study, authors evaluated obesity in adult lymphoma survivors and found that 61% patients gained an average weight of 10.4 pounds during the observation period. The increase in body mass index (BMI) was greater than in general population.[11,12] Another study observed dietary and weight changes after lymphoma treatment and noted an average weight gain of 8.96 kilograms on follow up.[13] The association between HL treatment and subsequent weight gain has not been studied among Pakistani patients previously. We therefore designed this study to retrospectively explore the association of HL treatment with subsequent changes in weight among a cohort of patients.

MATERIAL AND METHODS

In this study, we collected and analysed secondary data using the online hospital information system. We identified all adult patients who received treatment for HL between January 2010 and

December 2013 at our institute. A total of 470 patients were identified. The inclusion criteria were histologically confirmed Hodgkin Lymphoma, adult patients with age 18 years or more, and receipt of chemotherapy at our hospital. We excluded patients, who were diagnosed at our hospital, but received treatment elsewhere, patients who were lost to follow up before completing treatment, and patients whose weight at the start of treatment was not documented. Based on these criteria, 402 patients were included in the final analysis. This study was approved by the institutional review board of the hospital.

Medical records of all enrolled patients in study period were retrospectively analysed. Data collection included demographics, comorbidities, B Symptoms, histological type of Hodgkin lymphoma, stage of disease, response to treatment, weight in kilograms at initial presentation and then at 6, 12 and 18-month mark since the start of treatment. The B symptoms were considered to be present if there was a weight loss of more than 10% over the last 6 months, and the presence of fever of more than 38 Celsius and drenching night sweats.[14] Clinical data extracted using a structured *pro forma,* were coded and entered into Microsoft Excel. All observations were also cross checked by an independent investigator. Univariate analyses were done using Student's t-test or analysis of variance. Multivariable analyses were done using linear regression analysis. All statistical tests were two-sided with a 5% level of significance.

RESULTS

A total of 470 patients underwent treatment for Hodgkin Lymphoma during the study period at our centre. Out of these, 402 patients were eligible for inclusion in the current study. There were 286 (71.1%) male and 116 (28.9%) female patients (Table-1). The mean age at start of treatment was 31.3 years (range: 18–75). Most patients (96%) did not have any comorbidity that could affect weight while 13 patients (3.2%) had diabetes mellitus and 2 (0.5%) were hypothyroid. 67% patients had B symptoms at the time of presentation. The most common histological type of HL was a Nodular Sclerosing type (48.8%) followed by Mixed Cellularity type in 43.8% patients. Most patients (49.5%) were in stage IV disease followed by stage III (22.4 %), stage II (19.0%) and stage I (9.1%) at the start of treatment.

Progressive increase in weight was observed in patients after treatment (Table-2). The mean weight at the start of treatment was 61.8 kg and the weight gain from baseline (at start of treatment) to 6, 12, and 18 months after start of therapy was 3.0 (±4.4) kg, 7.1 (±6.3) kg, and 9.5 (±7.8) kg, respectively. Factors associated with weight gain at the 18 months are shown in table 3 and 4. Weight gain was significantly associated with the stage of disease, presence of B symptoms and complete response to treatment.

The age and sex of patients were not significantly associated with weight gain at 18 months. However, compared to patients in stage I at diagnosis, those with stage II, III and IV had 3.52 kg (95% CI: 1.3–5.8), 4.7 kg (95% CI: 2.7–6.6) and 4.7 kg (95% CI: 2.7–6.6) more weight gain, at 18 months post completion of therapy. Patients with complete response had statistically significant average weight gain of 12.95 kg (95% CI: 9.73–16.2) at 18 months compared to patients in partial response or no response to treatment. This suggests that stage of disease at diagnosis, presence of B symptoms and response to treatment were significantly associated with weight gain.

Table-1: Demographics of patients

Age in years	
Mean (Standard deviation)	31.3 (9.53)
Range	18 – 75
Sex; n (%)	
Male	286 (71.1)
Female	116 (28.9)
Comorbidity; n (%)	
None	386 (96.0)
Diabetes mellitus	13 (3.2)
Hypothyroid	2 (0.5)
Polycystic ovary disease	1 (0.25)
B symptoms; n (%)	
Present	269 (66.9)
Absent	133 (33.1)
Morphology; n (%)	
Nodular sclerosis	198 (48.8)
Mixed cellularity	178 (43.8)
Lymphocyte rich	13 (3.2)
Nodular Lymphocyte predominance	11 (2.7)
Lymphocyte depletion	6 (1.5)
Stage; n (%)	
1	37 (9.1)
2	77 (19.0)
3	91 (22.4)
4	201 (49.5)

Table-2: Weight change after start of treatment

	Mean (SD)	Range
Weight (kg) at start of treatment; (n=402)	61.8 (13.9)	30–108
Height (m); (n=402)	165.8 (8.9)	140–189
Weight change at six months (from the start of treatment); (n=402)	3.09 (4.49)	-22–22
Weight change at twelve months (from follow up at six months); (n=371)	3.83 (4.19)	-12–18
Weight change at eighteen months (from twelve months); (n=311)	2.47 (3.45)	-17–16
Weight change at twelve months (from start of treatment); (n=371)	7.1 (6.32)	-16–30
Weight change at eighteen months (from start of treatment); (n=311)	9.5 (7.8)	-17–36

Table-3: Clinical characteristics influencing weight change at 18 months from baseline (Results from t-test and analysis of variance)

	Mean (SD)	95% Confidence interval	*p*
Sex			
Male	9.56 (8.11)	8.47–10.65	0.84
Female	9.37 (7.11)	7.92–10.82	
B symptoms			
Present	10.4 (8.28)	9.27–11.52	<0.01
Absent	7.63 (6.37)	6.37–8.89	
Stage			
1	5.48 (3.96)		0.01
2	8.54 (6.68)		
3	10.51 (7.92)		
4	10.16 (8.49)		
Disease response			
Complete response	10.50 (7.02)	9.68–11.32	<0.01
Partial response / No response	-0.85 (8.34)	-4.15–2.45	

Table-4: Clinical characteristics influencing weight change at 18 months from baseline (Results from multivariable linear regression analyses)

	Coefficient	95% Confidence interval	*p*
Age	-0.07	-0.15–0.01	0.10
Sex (Male compared to females)	0.60	-0.96–2.17	0.45
B symptoms (Presence of B symptoms compared to absence)	3.01	1.35–4.67	<0.01
Stage of disease (compared to Stage I)			
Stage II	3.52	1.28–5.76	<0.01
Stage III	4.70	2.35–7.06	<0.01
Stage IV	4.66	2.67–6.65	<0.01
Complete response to treatment (Compared to partial or no response)	12.95	9.73–16.18	<0.01

DISCUSSION

Based on the results and statistical interpretation, it is observed in our study that patients with Hodgkin Lymphoma (HL) after treatment have a tendency to gain weight and this trend was progressive. The average weight gain at 18 months was 9.5 (±7.8) kg. The important finding was a strong association between weight gain and the presence of advanced stage of disease at time of diagnosis, B symptoms and complete response to chemotherapy.

Lynce *et al*, [11] studied weight gain in survivors of lymphoma and found that a survivor of lymphoma appears more likely to gain weight after treatment as compared to the general population. In this study, heterogeneous groups of HL and Non-Hodgkin Lymphoma (NHL) were monitored for a period of 18 months. About 61% of patient gained an average of 10.4 pounds weight after treatment of lymphoma and this weight gain was double compared to the general population.

Dietary and weight changes after treatment of lymphoma were studies by Nancy C[14] *et al* and they concluded that 62% patients gained 8.96 kg weight during follow up period. The majority of patients in their study reported that they had healthy dietary changes by eating more whole grains, vegetables and fruits after treatment as compared to before diagnosis of lymphoma.

Survivors of breast cancer also have shown a trend towards weight gain after treatment.[15] This weight gain in breast cancer patients, not only influence breast cancer specific survival, but also affects general health status. Weight gain after treatment in acute lymphoblastic lymphoma and its association with outcome has been evaluated in many studies. Marrisa *et al*[16] found that a decrease in weight during therapy is associated with decrease overall survival in children with ALL. Weight loss during cancer treatment was found to be associated with grave outcome in several cancers and is a powerful predictor of outcome in Lung cancer.[17] One recent study showed that weight gain during treatment of Lung cancer is indicator of clinical benefit.[18]

The pathophysiology of weight gain after treatment in HL patients has yet to be explored. The exact mechanism behind the observed weight gain in survivors of lymphoma is unclear. It may be related to systemic changes secondary to adipocyte cytokines production and systemic inflammation.[19] Life style changes, increase food intake and reduced habitual activity start after treatment of cancer. These may be contributing factors for weight gain after cancer treatment.[20]

Physical activity is reduced in cancer survivors. Courneya *et al*[21] studied physical activity in cancer survivors and concluded that only 21.4% of cancer patients remained active after treatment. Increase in weight, makes these patients high risk for developing cardiovascular diseases. Anthracyclines remain a key component of HL chemotherapy and they have well recognized association with cardiomyopathy. Obesity is an independent risk factor for cardiomyopathy among patient treated with doxorubicin.[22]

The strength of our study includes a large number of patients and we specifically evaluated only HL patients. In addition, all weight values used in our study were measured during routine clinical visits.

There were also some limitations of our study, such as the retrospective nature of study and we did not compare our results with a control group of healthy siblings.

CONCLUSION

Based on our study, a large number of Hodgkin Lymphoma survivors suffer from weight gain. An average weight gain at 18 months was 9.5kg. We found a statistically significant association between weight gain and advanced stage of disease, presence of B symptoms and response to therapy. Further studies are required to confirm these observations. There is also a need to investigate the aetiology of weight gain in survivors of cancer.

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Conflict of Interests: Authors have nothing to declare.

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