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Research Article

WEIGHT CHANGES DURING TUBERCULOSIS TREATMENT-IMPACT OF AGE, GENDER AND SITE OF TUBERCULOSIS-SINGLE CENTER STUDY.

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Abstract:

Objective: This study was conducted to document effect on body weight during of antituberculous therapy with impact of site of tuberculosis, age and gender of patient.

Study Design: Cross sectional study

Place & Duration: At Chest unit Bahawal Victoria Hospital Bahawalpur between November 2018 to April 2019

Methodology: The weight record was documented at start, first, second, fifth month and completion with age, gender and site of disease.

Results: Eighty-four patients enrolled. Body weight at the start of treatment was Range 25-90Kg (Mean 48.22+/-12.17) and at completion of treatment Range 28-89 Kg (Mean 52+/-12.31) . [Pulmonary Weight change P- (0.042)] and Body weight after first month of treatment is Range 26-92 Kg (Mean 48.80+/-12.26) [Pulmonary Weight change P- (0.000)] - Body weight after second month of treatment is Range 26-92.52 Kg (Mean 49.70+/-12.08) and Body weight after fifth month of treatment was Range 27-90 Kg (Mean 50.91+/-12.11)

The gender-based P Value for 1st Month weight Change Male - 0.016 Female- 0.000 and P Value At ATT completion weight Change Male - 0.224 Female- 0.011.

The weight changes in different sites with age were non-significant P>.05, for all recorded months.

Conclusion: Significant weight gain was seen in pulmonary tuberculosis and first month weight gain was statistically significant in both genders. Age related body weight changes were non-significant.

Keyword: Tuberculosis, Weight , Body, Gender, Age, Site of tuberculosis.

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INTRODUCTION:

Pulmonary tuberculosis has been named as consuming disease and weight loss is a cardinal feature of active disease¹. Simply monitoring weight changes tells us about the disease pattern as it's a clinical indicator of immunosuppression too¹. Inflammatory mediators such as tumor necrosis factor- (TNF), C reactive protein (CRP) and poor nutritional status are considered important factors^{2,3}.

These mediator's role in anorexia and cachexia was endorsed by evaluating antagonists of TNF, interleukin-6 (IL-6), leukemia inhibitory factor (LIF), ciliary neurotrophic factor (CNTF) and interferon- γ (IFN- γ) with resultant improvement in appetite thus weight gain². Protein energy malnutrition and micronutrients deficiency not only makes an individual prone to tuberculosis but this effect also becomes a feature during active disease until appropriate treatment is given that results in body weight stabilization along with proper commissioning of immune system³. However, it has been seen in certain areas that overweight is also being diagnosed and treated as TB⁴. This fact was clearly demonstrated, at Pokhara Nepal 11.35%, 49% in Ghana, more than 15% in centers of India, 29.4% in Brazil, 43% in Malawi and more than 42% in Tanzania were overweight or of normal weight at the start of treatment⁴.

Leptin is a prototype adipokine, is a product of ob gene, the 16-kDa and an appetite suppressant⁵. Its concentration is increased by inflammatory mediators reducing and also corresponds to fat mass thus same happens in tuberculosis^{5,6}.

The neglect of nutrition improvement and lack of weight gain during first month is associated with mortality and treatment failure^{7,8}. Twenty one percent mortality in severe malnourished patients was seen in comparison to 6.5% in mildly deficient patients of tuberculosis⁷. The weight gain was better obtained while on treatment in those societies who were more educated and showed adherence to nutritional advices and DOTS components⁹.

The mechanism of weight gain is not completely understood particularly for multidrug resistant tuberculosis as inspite of increased calories and nutritional support few patients still didn't regained the fat free mass¹⁰. Initial drastic weight loss in early course of disease was proposed for this reason¹⁰. Maybe this is the ambiguity for lack of weight gain in extra pulmonary tuberculosis as well¹⁰. All types of measures ranging from increased food intake or adding gradual increased fat supplements in diet resulted in favorable weight gain with appropriate therapy¹⁰.

Similarly, the above proposed theory of weight loss due to alone leptin has also been challenged proposing some other mechanism involved¹¹. Gender was never a significant factor in weight gain during treatment inspite of fact that fat mass was major contributor of weight gain in females¹². This is a known fact that malnourished and underweight individuals fails to provoke immune system enough to combat tuberculosis and hence may ends up as high mortality group¹³.

The age has been the factor that effects the outcome of many diseases. Similar effect was seen at a study conducted at an American hospital where increasing age particularly more than 60 was associated with failure to weight gain in tuberculous patients under treatment¹.

A study conducted at Zanzibar Tanzania to document weight changes during antitubercous therapy with site of tuberculosis involvement and that study concluded with no statistically significant change between pulmonary and extrapulmonary tuberculosis weight changes with treatment¹⁴.

We opt to conduct this study as many studies showed significance and measurement of body weight as a predictor of tuberculosis outcome⁹, this fact is discussed in detail in discussion section. Moreover it can be measured in all patients, it consumes no time in providing useful information, equipment is economical to purchase and is present at all sections of hospitals and even few keep domestically, patient has no hesitation to stand on weighing machine and moreover no training or expert staff is required for its measurement. Moreover, we can assess its significance in our community considering age, gender of patient and whether pulmonary or extrapulmonary tuberculosis was being treated.

Considering all these facts we conducted this study to document the weight changes during antitubercous therapy and its impact on age, gender and site of tuberculosis in patients at south Punjab.

METHODOLOGY

Cross sectional study conducted at chest unit Bahawal Victoria Hospital Bahawalpur between November 2018 to April 2019 - Those patients were enrolled whose treatment was completed/cured. The weight record was documented at start of treatment and first, second, fifth month and at time of completion. Other variables study included were age of patient, gender, site of involvement of active tuberculosis.

Data was extracted for patient demography (age, gender), treatment data (antituberculous therapy months and weight change) and disease characteristics (site of active tuberculosis treated) from treatment tickets. Following patients were included in study

1. Those who completed full treatment and survived.
2. Non-diabetics
3. Non-smokers
4. Those who took first line antituberculous therapy.
5. Must not be on injectables (for questionable compliance of injectables of 2-4 months)

Follow-up information was obtained after first, second, fifth months and at time of treatment completion. Recorded data was broken down to arms of age, gender, site of tuberculosis involvement. Body weight was documented in kilograms (KG) assessed by nursing staff during each visit of said months. Changes in body weight were computed by comparing weights of subsequent months with body weight at start of treatment. Age in years were divided into following groups

- 1- 14-20
- 2- 21-40
- 3- 41-60
- 4- 61-75

All variables were entered in SPSS. Patient baseline bodyweight was compared between four variations during antituberculous therapy i.e. at first, second, fifth month and at time of completion. The chi square test was used for categorical variables. P value <0.05 was taken as significant.

RESULTS:

Eighty-four patients were included in study, among which 38 (45.2%) were males and 46 (54.8%) were females. Age ranged from 14 to 75 yrs.

Sites of tuberculosis involvement were pulmonary 64.3% (n-54), pleural effusion 10.7% (n- 9), tuberculosis meningitis 4.8% (n-4), cervical Lymph

nodes 3.5% (n- 3), abdominal 2.4% (n-2), abdominal Lymph nodes 2.4% (n-2), pelvic 1.2% (n-1), breast 1.2% (n-1) and skin 1.2% (n-1).

Gender based site was, for TB in females as 2.17% (n-1) Abdominal, 2.17% (n-1) Abdominal Lymph nodes, 2.17% (n-1) Pelvic, 2.17% (n-1) Breast, 4.34% (n-2) Caries spine, 6.52% (n-3) pleural effusion, 8.69% (n-4) meningitis, 10.86% (n-5) Cervical lymph nodes and 60.86% (n-28) pulmonary tuberculosis. For TB in males body sites were as 2.63% (n-1) Abdominal, 2.63% (n-1) Abdominal lymph nodes, 2.63% (n-1) Caries spine, 2.63% (n- 1) Skin, 5.26% (n-2) Cervical lymph nodes, 5.26% (n-2) Pleural effusion and 68.42% (n-26) Pulmonary TB.

Body weight at the start of treatment was Range 25-90Kg (Mean 48.22+/-12.17) and Body weight after first month of treatment is Range 26-92 Kg (Mean 48.80+/-12.26) [Pulmonary Weight change P- (0.000)] - Body weight after second month of treatment is Range 26-92.52 Kg (Mean 49.70+/-12.08) and Body weight after fifth month of treatment was Range 27-90 Kg (Mean 50.91+/-12.11) and at completion of treatment Range 28-89 Kg (Mean 52+/-12.31) . [Pulmonary Weight change P- (0.042)] (Site based weight changes in Table-i)

Body weight at the start of treatment and at completion of treatment, P Value less than 0.05 of significance level was only for Pulmonary Weight change (0.042) while body weight at the start of treatment and at completion of first month of treatment, P Value less than 0.05 of significance level was only for Pulmonary Weight change (0.000) -

The gender-based weight changes (Table-ii) for 1st Month weight Change P Value Male - 0.016 and Female- 0.000 while P Value at ATT completion weight Change Male - 0.224 and Female- 0.011 - The weight changes in different sites with age (Table-iii) P Value at Start and completion of first month ATT was > .05. and for weight change at Start and completion of ATT was > .05.

Table I – Body weight changes of patients on ATT with Site of involvement

SITE	Start	1 st month	2 nd month	5 th month	Completion
Pulmonary Mean	46.66	47.13	47.88	49.25	49.90
St Dev.	12.37	12.44	12.25	12.72	13
% Increase	-----	1.007%	2.61%	5.55%	6.94%
Pleural Effusion Mean	51.88	51.44	51.5556	52.6667	54.6667
St Dev.	8.75	8.14	8.20	8.23	8.36
% Increase	-----	-0.84%	-0.63%	1.50%	5.35%
Cervical LN Mean	47.1667	49.1667	50.3333	51.8333	54.1667
St Dev.	4.62	5.41	4.54	4.53	4.99
% Increase	-----	4.24%	6.72%	10%	14.84%
TBM Mean	50.5000	51.0000	51.2500	53.2500	55.7500
St Dev.	9.43	9.89	10.40	8.61	7.50
% Increase	-----	0.99%	1.48%	5.44%	10.39%
Abdominal LN Mean	43.5000	46.5000	49.5000	51.0000	52.5000
St Dev.	3.53	7.77	9.19	9.89	10.60
% Increase	-----	6.89%	13.79%	17.24%	20.68%
Abdominal TB Mean	29.5000	31.5000	34.5000	37.0000	36.0000
St Dev.	3.53	3.53	2.12	4.24	.00
% Increase	-----	7.54%	16.94%	25.43%	22.03%
Caries Spine Mean	53.5000	54.5000	55.5000	56.0000	55.0000
St Dev.	9.19	10.60	10.60	11.31	9.89
% Increase	-----	1.92%	3.73%	4.67%	2.80%
Skin TB Mean	62	62	62	62	63
St Dev.	-	-	-	-	-
% Increase	-----	0%	0%	0%	1.61%
Breast TB Mean	62	64	64	62	62
St Dev.	-	-	-	-	-
% Increase	-----	3.22%	3.22%	0%	0%
Pelvic TB Mean	43	46	43	41	44
St Dev.	-	-	-	-	-
% Increase	-----	6.97%	0%	-4.65%	2.32%

P Value for Pulmonary Weight gain (0.042) (only pulmonary weight changes were less than .05)

Table II Weight changes – Effect of Gender

Gender	Start	1 st month	2 nd month	5 th month	Completion
Male Mean	53.03	53.86	54.64	56.15	56.84
St Dev	11.38	11.37	11.25	11.38	11.78
% increase	-----	1.56%	3.03%	5.88%	7.18%
Female Mean	44.26	44.63	45.63	46.58	48
St Dev	11.44	11.46	11.30	11.07	11.38
% increase	-----	0.83%	3.09%	5.24%	8.45%

P Value for 1st Month weight Change Male - 0.016 Female- 0.000
P Value at ATT completion weight Change Male - 0.224 Female- 0.011

Table III -Weight changes on ATT with Age groups .

Age groups (yrs)	Start	1 st month	2 nd month	5 th month	Completion
14-20 Mean	39.84	40.57	41.78	42.47	43.89
St Dev	8.26	8.18	7.13	6.51	6.94
% Increase	-----	1.83%	4.86%	6.60%	10.16%
21-40 Mean	51.28	51.56	52.50	54.36	55.52
St Dev	12.37	12.76	12.40	11.37	11.63
% Increase	-----	0.54%	2.37%	6%	8.26%
41-60 Mean	50.21	50.96	51.71	52.25	53.14
St Dev	12.93	12.76	13.17	13.15	13.56
% Increase	-----	1.49%	2.98%	4.06%	5.83%
61-75 Mean	49.54	50.18	50.81	53.27	54.09
St Dev	10.06	10.91	10.81	13.28	13.20
% Increase	-----	1.29%	2.56%	7.52%	9.18%

P Value for weight change at Start and completion of first month ATT was > .05 for all age groups.

DISCUSSION:

Our study was cross sectional and the only in our south Punjab area for assessing weight changes during antituberculous therapy. This study showed that patients could gain, lose or maintain their weight throughout antituberculous treatment.

We also demonstrated that statistical significance change in weight during therapy was only associated with pulmonary tuberculosis (P value-0.042) while for other sites in spite of weight gain and clinical improvement, statistical significance was not seen. Similar results were seen from intensive phase one month till completion of treatment with statistical significance of ($p < 0.001$) from a study at community-owned healthcare system in Houston, Texas, USA¹⁵ where majority of patients were of pulmonary involvement. The exact reason causing weight loss in TB and

subsequent weight gain after treatment were discussed in introductory portion of this article with some mediators held responsible for it and yet concluding that mechanisms were not completely understood^{10,11}. As recently ghrelin a 28 amino acid peptide level has been found different in tuberculous patients along with leptin. Moreover, levels of inflammatory cytokines for example tumor necrosis factor alfa, interferon gamma and Thi 1 type cytokine, are also being held responsible for weight loss¹¹. This Texas study also showed that sputum smear positive, cavitary and extensive diseases with appropriate treatment showed better weight changes¹⁵. However, such radiological variables were not among inclusion criteria of our study and we also excluded diabetics and malignancy patients.

One of the limitation of our study is its retrospective nature so no information was available on dietary intake in reviewing treatment tickets but as south Punjab is an area where people are not much health literate so dietary deficiencies do contribute towards failure to thrive in ill or normal looking individuals therefore the possibility that inadequate nutritional intake may well be the factor in extra-pulmonary tuberculosis for non significant weight gain¹⁰. The same possibility has been postulated even in developed country for failure to achieve weight gain¹⁵.

The important fact of weight gain revealed in our study during first month of intensive therapy for pulmonary tuberculosis at significant level (P-Value 0.000) and further weight gain at completion was also significant thus showing gradual and sustained weight gain throughout the months till completion. In study conducted at Houston Texas USA identical response of linear increase in weight was observed with passing months till completion¹⁵. Thus, emphasizing positive role of completion of uninterrupted therapy.

It's a known fact that first month increase of weight is associated with best outcome and the cohort who lose weight are more likely to die or end up as treatment failure and sent for multi drug resistant tuberculosis testing¹⁶.

The significance of our study is further endorsed by other many clinical researches works where changes in weight a simple tool to measure, has been postulated as a factor not only to predict treatment response but also as predictor of mortality and multi drug resistant tuberculosis. So rather than waiting for sputum results, which may take weeks for a culture to report this simple tool can guide us about treatment outcome and predicted mortality¹⁷. That's an important contribution for patient assessment at resource constrained areas. The same fact was described in the ancient Greek era where it was names wasting disease (phthiasis) so no weight gain means active disease consuming the body showing treatment failure either due to inappropriate therapy or other reasons¹⁸.

However opponents aroused from Tanzania nullifying weight loss as clinical parameter of poor outcome but they demonstrated few important facts that gender, hospital stay and HIV positive tuberculosis patients with good nutritional support can be appropriately cured¹⁵.

Appropriate body recovery measured as total arm muscle circumference, fat mass, serum albumin, bone minerals and protein mass were beyond scope of our disease.

Although the disease progression, outcome and even clinical signs are different in elderly tuberculous patients, but in our study though weight gain was a feature in elderly population as well but that gain was not statistically significant. At Peshawar Pakistan a clinical trial showed that failure to gain weight in elderly population was a poor prognostic factor¹⁹. At District Tuberculosis center, Yavatmal, India, tuberculosis outcome was similar in elderly people and young age group, this is in comparison to our study regarding statistically equal significance weight changes in both. However, in an African study high default rate in elderly effected the outcome²⁰. However, assessing extent of tuberculosis, comorbidities and documenting default rate was not aim of our study. As we discussed earlier in this article about role of Leptin in tuberculosis weight changes^{5,6}. While considering the gender leptin level were reduced in both genders with tuberculosis otherwise in health, they are higher in females²¹. Serum procalcitonin levels have also been proposed as factor inversely proportion to weight changes with no gender difference²².

In our study the weight gain after first month of intensive therapy was statistically significantly altered in both males and females while at completion only females achieved significant weight change (P-Value-0.01) though males also continue to improve body weight with no significance (P-Value-0.224). This finding is contrary to the outcome at Mashhad University of Medical Science, Mashhad, Iran, where both genders showed significant changes in both cured and treatment completed groups²³. In our study maybe fat mass was major contributor of weight gain in females^{10,12}. But needs further studies to evaluate this difference.

CONCLUSION:

Our study demonstrated that weight variation during intensive phase was significant in both genders groups in pulmonary tuberculosis then extrapulmonary tuberculosis. However for gender balanced manner weight change was transient and was not achieved for males at the end of study. Furthermore, the variation of weight change for all sight at intensive phase and at completion with regard to age was not significant inspite of clinical improvement.

RECOMMENDATIONS

Further studies are planned in future to evaluate the reasons of such discrepancies and to evaluate why tuberculosis happened in normal weight or over weight individuals⁴

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None.

Conflicts of Interest

The authors have no relevant conflicts of interest to disclose.

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