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RESEARCH ARTICLE

RAMADAN FASTING AMONG MUSLIM CANCER PATIENTS RECEIVING OUTPATIENT CHEMOTHERAPY AND BIOLOGICAL THERAPY: BEHAVIOUR & SIDE EFFECTS, A CROSS SECTIONAL STUDY.

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Abstract

Background and objectives:-Ramadan fasting is the fourth pillar of Islam. Several studies showed that supervised intermittent fasting may influence the course of different diseases favourably. However, few studies have examined the feasibility of Ramadan fasting in cancer patients who are receiving chemotherapy. This study aims to assess the behaviour of cancer patients who received chemotherapy and/or biological therapy -at King Abdulaziz University Hospital (KAUH)- toward fasting and to compare chemotherapy side effects in fasting and non-fasting states.

Methods:- A structured questionnaire was used to interview adult cancer patients who received single day intravenous -with or without oral- chemotherapy and intravenous biological therapy during and after Ramadan at day care unit of KAUH. Assessment of chemotherapy-related side effects was graded based on National Cancer Institute Common Terminology Criteria for Adverse Events. The side effects were compared in the same patients after receiving chemotherapy and/or biological therapy during fasting and non-fasting states.

Results:- A total of 77 cancer patients were surveyed.fifty five (71.4%) were females. The mean age was 50.4±SD14.9years.fifty nine (76.6%) patients fasted during Ramadan, 37% were able to complete fasting throughout the month except on the day of therapy. The likelihood to fast was significantly associated with patient's age (P=0.003) and the number of treatment cycles (1 vs.2cycles) (P=0.008).The severity of chemotherapy-related side effects was not affected by fasting status.

Conclusion:- Patients of young age and those who receive single cycle of intravenous chemotherapy are more likely to fast. There is no significant increase in chemotherapy or biological therapy side effects while fasting the days of Ramadan. Patients should be encouraged to discuss this issue with their physicians to improve the awareness and compliance to chemotherapy.

Introduction:-

Ramadan is the ninth month of the lunar calendar. Ramadan fasting is the fourth pillar of Islam. Fasting during the holy month of Ramadan is obligatory for all adult Muslims who are able to fast. Fasting includes abstinence from food and drink from dawn to sunset. Duration of fasting varies between countries ranging from 9.5 to 21 hours during the day. It also changes over years in the same country. In Saudi Arabia, duration of fasting is about 15 hours.

Fasting (no calorie intake) results in ketogenesis, promotes potent changes in metabolic pathways and cellular processes such as stress resistance and lipolysis. It also induces a wide range of changes associated with cellular protection. Several studies examined the effect of both caloric restriction and intermittent fasting on diseases and showed that supervised fasting is associated with deceleration or prevention of some chronic degenerative and inflammatory diseases, in addition to chronic pain syndromes, hypertension, and metabolic syndrome (1).

Muslim Patients with cancer differ in their abilities and willingness to fast. A cross-sectional study which was conducted among 102 Muslim cancer patients at the National Cancer Institute in Egypt revealed that 40% of patients did not fast at all during Ramadan, the remaining were partial and complete fasters. Only 46% of patients sought the treating oncologist advice on whether they could fast. Female patients, those with performance status 0 to 1, those whose disease was a non-metastatic solid tumour, and those receiving non-intravenous chemotherapy as outpatients were more likely to fast than their corresponding counterparts (2). Similar results were found in a Turkish cross sectional study which assessed the extent of fasting status in cancer patients. However, only 20.8% of all patients have consulted their physician about whether or not to fast (3).

Fasting also seems to influence cancer sensitivity to treatment in animals .A number of experimental studies on mice showed that short term fasting make cancerous cells more susceptible to chemotherapy than they otherwise might be and provide protection to normal cells against high dose chemotherapy, an effect called "differential stress resistance". Mice with different types of cancer treated with a combination of chemotherapy and fasting had better survival chances than those treated with either fasting or chemotherapy alone, they also had smaller tumours (4)(5).

Whereas in humans ,Safdie et al described 10 cases of patients with different malignancies who had voluntarily fasted prior to and/or following chemotherapy, with no detrimental side effects related to fasting .The Results of the study suggest that fasting in combination with chemotherapy is safe and feasible(6). In a pilot study -conducted by Badar T and colleagues- on 11 cancer patients who were receiving chemotherapy at king Fahad medical city, Riyadh, Ramadan fasting was found to be safe and well tolerated. It resulted in overall reduction in side effects of chemotherapy compared to non-fasting (7).Both studies are limited due to the small sample size.

Our study aims to assess the characteristics and the behaviour of different Muslim cancer patients who received chemotherapy and/or Biological therapy -at King Abdulaziz University Hospital(KAUH)- toward fasting in the days before and after chemotherapy or biological therapy and to compare chemotherapy side effects in fasting and no fasting states.

Methods:-

Adult cancer patients who received single day intravenous -with or without oral- chemotherapy and intravenous biological therapy during Ramadan (18/6/2015-16/7/2015) at KAUH day care unit and after Ramadan (between July and August 2015) were interviewed.

Cancer patients who received oral chemotherapy alone, or those not on 3 or 2 weekly regime and those whose last chemotherapy cycle was in Ramadan were excluded. Also non-Muslim, non-Arabic and non-English speakers were excluded.

A structured questionnaire was designed to fulfill the study objectives. It was filled by the interviewer for eligible patients**.** We obtained the following data through the questionnaire which consisted of 5 parts: first part contained demographic data that included age, gender, career, level of education. Second part included questions about patient attitudes and characteristics including number of fasting days, reasons for non-fasting, discussing the issue of fasting with the treating physician and sheikh. Third part contained information about the diagnosis, duration and stage of disease, and associated co-morbidities. Fourth part included types of treatment received in Ramadan and one month before or after Ramadan (chemotherapy, radiotherapy, hormonal therapy and surgery) and the last part contained National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE, version 4.0) which is used to describe severity of organ toxicity for patient receiving cancer therapy. We aimed to assess gastrointestinal side effects mainly. The side effects were compared in the same patient after receiving chemotherapy and/or biological therapy during fasting and non-fasting states. Patients were consented. All questioners were validated and coded to avoid identification of the subjects. They were kept in a close cabinet to ensure confidentiality.

Statistical analysis:-

The data was analysed using Statistical Package for the Social Sciences software program (IBM SPSS statistics v. 20.0). Independent sample T test was used to assess differences in ages and duration of disease between the fasting and non-fasting groups, also Man Whitney U test was used to assess differences in side effects severity in same patients during fasting and non-fasting states. Chi square test was used to assess the association between each of gender, employment, number of cycles of therapy, stage of cancer and fasting status. A P value of .05 or less was considered significant.

Results:-

A total of 77 patients were eligible for participation in the study. Fifty Five (71.4%) were females and twenty two (28.6%) were males. The mean age of the participants was 50.4±SD14.9 years ranging from 18 to 85 years, 26% of them were employed and 74% were unemployed .Thirty one patients (40.3%) received secondary education, twenty six (33.8%) received tertiary education, eight (10.4%) received primary education, another eight patients could read and write and four (5.2%) were illiterate. Most patients (64.9%) received chemotherapy or biological therapy once in Ramadan, 24 patients (31.2%) received therapy twice and only 3 patients (3.9%) received it three times. 37.7% of all patients consulted their physicians about fasting. Most of the times (72.4%); the physicians advised their patients against fasting, whereas in 17.2% of cases, the physicians left the decision of fasting to the patients according to their physical abilities.15.6% of patient's sought the opinion of a Sheikh regarding fasting; most of them (66.7%) were advised to fast if they could tolerate it.

Eighteen patients (23.3%) did not fast any day during Ramadan, whereas fifty nine (76.6%) fasted. The number of fasting days ranged from 2 to 28 days with mean 21.7±SD7.8days and of non-fasting days was 6.6 ±SD7.6 days (excluding the days of menstruation in 5 females).Twenty two patients (37%) were able to complete fasting throughout the month except on the day of therapy. The most common reason for fasting break among those who fasted was receiving therapy (57.6%). Among the 18 patients who didn't fast; 4 patients (22.3%) didn't fast as per the physician's advice, an additional 4 (22.3%) didn't fast due to their chronic diseases (mainly Diabetes Mellitus, Hypertension and Anaemia), 3 patients (16.7%) said that they experienced side effects of chemotherapy or biological therapy whereas another 3 (16.7%) said they were unwilling to fast, 4 patients (22.3%) didn't fast due to side effects plus their physician advice, combined with chronic illnesses. The side effects included: fatigue, pain, vomiting, nausea, diarrhoea, dyspepsia, and body rash. Fifty-nine patients (76.6%) received Chemotherapy in Ramadan and the month before or after, as 10 patients (16.9%) started their first cycle in Ramadan whereas 24 (41.4%) had their 3rd or 4th cycle. Patients received different chemotherapy regimens as shown in (table 2). Fifteen patients (25.4%) received oral chemotherapy in addition to intravenous and the majority of them (81.3%) took the oral pills for full 14 days after feast and before dawn. All 15 fasted except one patient. Furthermore, twenty patients (25.97%) received biological therapy (Transtuzumab) in Ramadan and the month before, 2 of them also received chemotherapy.

Among patients who fasted, 44 (74.6%) received chemotherapy while 15 (83.3%) of those who didn't fast received chemotherapy. The majority of fasting patients who received chemotherapy (63.6%) had one cycle of therapy in Ramadan whereas the majority of patients who received chemotherapy and didn't fast (66.7%) received two cycles of therapy (P=.03).

A statistically significant association was found between patients' age and their fasting status (P=.003). Patients who didn't fast at all were older (mean=59.4±SD12.8) compared to those who fasted (mean=47.6±SD14.5), with a mean difference of 11.8 years (95% CI, 4.2 to 19.3). Patients' gender and employment status were not statistically significant to the fasting status. Similarly, the severity of chemotherapy-related side effects reported by the patients were not related to the fasting state; pain (P=.56), mouth sores (P=.38), nausea (P=.48), vomiting (P=.74), difficulty swallowing (P=.82), diarrhoea (P=.22) and fatigue (P=.97). The most common cancer type was breast cancer (51.9% in total & 70.9% in females), followed by colorectal cancer (19.5% in total & 52.4% in males) and lymphoma (13%). Cancer stage III was the most frequent stage among all diagnoses (53.4%). 81.2% of patients with stage IV disease fasted. However, no statistically significant association between cancer stage and fasting was demonstrated (P=.34) (table.1).

Table 1.Analysis of different variables (age, gender, employment status, cancer stage, number of treatment cycles, cancer type and physician consultation) on the likelihood of fasting in Ramadan.

Variables	Total (77)%	Fasting (59)%	Non-fasting(18)%	P
Age				
< 60	57(74%)	48(81%)	9(50%)	0.07
> 60	20(26%)	11(19%)	9(50%)	
Gender				
females	55(71.4%)	41(69%)	14(78%)	0.49
males	22(28.6%)	18(31%)	4(22%)	
Employment				0.24
employed	20(26%)	17(28.8%)	3(17%)	
Unemployed	57(74%)	42(71.2%)	15(83%)	
Cancer stage (19 unstaged)				0.34
Non-metastatic	42(72%)	30(70%)	12(80%)	
metastatic	16(28%)	13(30%)	3(20%)	
Number of cycles in Ramadan				
1	50(65%)	43(73%)	7(39%)	0.008
>1	27(35%)	16(27%)	11(61%)	
Physician Consultation				
yes	29(38%)	19(32%)	10(56%)	0.073
No	48(62%)	40(68%)	8(44%)	
Cancer type				
Breast cancer	40(52%)	32(54%)	8(44%)	
Colorectal cancer	15(19%)	14(24%)	1(5.5%)	0.006
lymphoma	10(13%)	6(10%)	4(22%)	

Table 2.Chemotherapy regimes administrated to the study cohort

Chemotherapy regimens	Percentage	Chemotherapy regimens	Percentage
Docetaxel	18.6	Docetaxel/Carboplatin	3.4
XELOX	15.3	ECX	3.4
AC	13.6	Cisplatin/Irintotecan	3.4
Gemcitabine	8.5	CHOP/R	3.4
ABVD	8.5	Cisplatin/Docetaxel	1.7
XELIRI	5.1	FEC	1.7
CVP/R	5.1	Cisplatin	1.7
Capcitabine/Bevacizumab	3.4	TCH	1.7
TC	3.4		

Discussion:-

In Saudi Arabia, as a Muslim country, the majority of cancer patients were fasting while receiving chemotherapy during Ramadan. Chemotherapy has limited differential activity against cancerous and non cancerous cells which result in related side effects. Possibly, these side effects may influence the patients' attitude toward fasting. Patients may anticipate exaggerated chemo-related side effects which interfere with their willingness to either fast or receive chemotherapy. Conversely, fasting has shown to be an enhancing strategy for cancer treatment by decreasing side effects while protecting normal cells (4). Several studies have shown that 20%-40% reduction in calorie intake protects the host against toxins and delays the growth of tumours (8,9). In our study, no patient reported serious complications during fasting. Many patients did not report any change in the severity of chemotherapy-related or

/biological therapy-related side effects during Ramadan fasting. A claimed detrimental effect of fasting on blood pressure and energy level was reported in one study (10) but our fasting patients did not report any symptoms of increased thirst, loss of energy or hypotension. Each patient on the study served as a control for him/herself in regard to therapy side effects assessment. Comparing side effects in the same individual in fasting and non-fasting states provided accurate evaluation. A considerable proportion of patients with stage IV cancer were able to fast and cancer stage did not influence the ability of patients whether to fast or not. The observation of breast cancer being associated with increased fasting likelihood might have been confounded by the fact that significant proportion of breast cancer patients were receiving single agent biological therapy (Trastuzumab) that has favourable side effect profile in comparison to chemotherapy, which was not the case in other malignancy types.

Young patients and those who received single cycle of intravenous chemotherapy were more likely to fast. The decreased likelihood of fasting with increasing age is attributed to the co-existing chronic illnesses rather than the side effects of therapy. Chronic illnesses accounted for the second most common reason for no fasting with Diabetes mellitus and hypertension being the most common ones. Gender, educational level and employment status did not show to impact the likelihood of fasting

Physicians tend to advice their patients against fasting, but patients' adherence to such advice was variable. Many patients were able to fast smoothly in spite of the treating physicians' recommendation, implying that physicians might have misapprehend their patients' capability or overestimated the potential side effects with fasting. Lack of sufficient evidence and objective measures to assess cancer patients' ability to fast may have contributed to this and our study may help to provide some guidance into this.

Conclusion:-

Ramadan fasting for cancer patients who are receiving chemotherapy may represent a concern with subsequent poor compliance and less favourable outcomes. The available literature examining this issue is limited and not consistent. Our study examined the feasibility and tolerability of fasting while on chemotherapy. Fasting the holy month of Ramadan is feasible and tolerable for cancer patients who are receiving outpatient chemotherapy or biological therapy. There was no significant increase in chemotherapy-related side effects with fasting. Patients of young age and those who receive single cycle of intravenous chemotherapy are more likely to fast. Patients should be encouraged to discuss this issue with their treating oncologist to improve the awareness and compliance to therapy.

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