Chapter Five:

Discussion, Conclusion and Recommendation

5.1 Discussion:

The Prostate Specific Antigen can be an excellent reference as a cancer biomarker in order to evaluate the outcome of prostate cancer treatments (Surgery &Radiotherapy) radiotherapy has been selected in this study. The normal Reference values of PSA is range from 0 up to 4 ng/ml in respective researches**(Jamal,1997)**, if the value increased above this reference, it may indicateof an existent disorders like(BPH, Neoplasia ,inflammatory Disorder..etc). (Omer, Yousef 2013) in trial to determine of PSA normal level in Sudanese patient found thatage group with high PSA level was (56-66) years with relative level 80.7 ng/ml, histopathological had a high mean of PSA level was adenocarcinoma with relative level 56.1 ng/ml.

At mean of follow-up of 2 months after radiation therapy, the PSA main level was (87 ± 48.6 ng/ml) at time of presentation PSA1, (13.4 ± 15.6 ng/ml) and after surgical operation PSA2 was (17.1 ± 24.1 ng/ml) for both types of surgery(Partial & Total Removals), Partial removals of prostate cancer was dominant in 152 patients as in table (4.1).

A significant correlation between PSA1-PSA3 determining using T-paried sample test with t-=19.8 and P=0.000 , with difference in means = (66.8±46.5ng/ml).Also pair sample t-test demonstrated significant difference between PSAs levels before and after both radiotherapy and surgery at p=0.000 for both test while the means difference between PSA1 and PSA2 to 70.7ng/ml and equal to 66.8 ng/ml for PSA1 and PSA3 as showed in table (4.8).

Prostate Specific Antigen was also reduced to recommended level (1-4ng/ml) in 45 patients represented (23.3%), 46 patients (11.4%) , below (1ng/ml) in 48 patients (24.8%), 22 patients (11.4%) , unfortunately the majority of Patients have PSA levels above (4ng/ml) 100 patients (51.8%) and 125 patients(64.7%)after Radical radiation therapy with dose range from 4500 to 5000 Gy and surgical removal respectively that due to delay of follow up 2 months after end of radiation, the majority of patients have partial removal (152) and long interval between Surgery and radiation therapy course (3 months was Privilege) Tables (4.5) . Stamey& Kabalin, (1989) foundedDuring year 1 after radiotherapy prostate specific antigen levels were decreasing in 82 per cent of the patients to recommended levels but only 8 per cent continued to decrease beyond year ,1 of 80 patients

observed greater than 1 year after completion of radiotherapy 51 per cent had increasing values and 41 per cent had stable values.

The PSA level at time of diagnosis was 60-150 ng/ml in 114 patients represented 59%, 64 patients (33.1%) PSA level was less than 60 and 15 patients (7.7%) with PSA level more than 150ng/ml as in table (4.5) which is close to reference levels (56.1ng/ml) mentioned in (Omer and Yousif ,2013). There was a relationship between PSAs different levels, PSA1 and PSA2 have a direct relation, As patients PSA1 was increased it will be high Also after surgery by 0.47ng/ml/ng/ml as in figure (4.1), Another an inverse relation between PSA2 and PSA3 was noted, so for higher PSA2 a lesser PSA3 levels by 0.102ng/ml/ng/ml as figure (4.2). In addition as PSA1 levels are increased PSA3 levels is decreased by 0.38ng/ml/ng/ml as in figure (4.3).

Moreover, Stage is an crucial aspect in treatment of patient, cancer control and treatment response; cancer with early stage have good outcome and overall survival than those patients with late stage, about 130 patients (67.4%) with stage 2 and only 63 patients (32.6%) with stage 3 as in table (4.4) – figure (4.5). Prostate Specific Antigen significantlydiffer for each stage according to the study there is a significant differences among study

population for PSA before the surgery and radiotherapy at P=0.000 (CL=95%) where for 130 patients PSA=(64.04±18.8ng/ml) for stage two and (125.8±46.8 ng/ml) which were 62 patients having stage three while this reduced totally to lower level after surgery PSA2 and stage two in radiotherapy and higher reduction rate after surgery comparing with radiotherapy as in figure (4.5), table(4,6). Thisstronglycorrelated with long interval between surgery and radiotherapy or rest period after completion of treatment courses because of less availability of diagnostic machines as in table (4.6)-(4.9). Nevertheless, there is strong correlation noted between reduction of PSA and stage after both treatment modalities (P=0.231 for surgery, P=.757 for radiotherapy) as in table (4.9) fig (4.7) and 4Fig(4.10-4.11) respectively

Also, PSA1 was highest for stage III with mean ± Std of (125.8±64.8)ng/ml while for stage II was (64±18.8) ng/ml as intable(4.4).

 The lowest level of PSA2 was (12.4±13.2)ng/ml for stage II and (15.3±20)ng/ml for stage III as in table(4.4). In addition PSA3 level was low in stage II with value of (17±23.2)ng/ml and higher in stage III with (18.13±26.7)ng/ml as stated in table(4.4), that confirmed the direct relation between the tumor Stage and PSA levels. The following four prognostic groupings were defined: group I, PSA   4ng/ml , any grade; group II, 4

<PSA   20, grades 2-6; group III, 4 < PSA   20, grades 7-10; group IV, PSA > 20, any grade (Gunar et al. 1995)

Age factor also affected the PSAs levels because that the older age the higher PSA levels as described in figure (4.8), a relative values founded for patient younger than 50years was 2.5ng/ml and more than 70 years was 6.5ng/ml (Brawer, 1998).

In addition, the number of patients were 9 patients (4.7%) for age group 1(39-50 years) , 26 patient (14%) for age group 2(51- 60years), 75patients (38.9%) for age group 3(61-70years) , 63 patient (36%) for age group 4 (71-80 years) and finally 20 patients (10%) for age group 5 (81-90 years) as in table (4.7).

 There were eight age groups, 5 patients in group1 (39-45.5 years) represented 2.5 per cent, with 74.8, 26.4 and 25.6 ng/ml PSA1,2,3 Respectively. Group2 (45.5-51.5years) 3 patients about 1.2 per cent have PSA1,2,3 levels 108.5,33.9, 3.7ng/ml respectively, this is the lower PSA3 level in study 1-4 ng/ml. Group 3(51.5-57.5 years) contained 5 patients 2.5 per cent with PSA12,3 108.5, 18.1 and 6.9 ng/ml respectively. Group 4 (57.7-64 years) with 35 patients about 17.5 per cent have PSA1,2,3 levels 83,15.2,20 ng/ml , therefore the most common was group 5 (64-70 years)

represented 61 patients about 30.5 per cent with 75.4, 9.6 and 17.5 ng/ml for PSA1,PSA2 PSA3 respectively, Group 6 (71-77.5years) have 48 patients about 24 per cent which have PSA1,2,3 about 83.7,11.6 and 19.3ng/ml respectively as in table (4.7)& fig(4.4).

Therefore, mean age for study was (69.1±9.4) years for patients from 39 up to 88 years old which had been studied as mentioned in table (4.2). The mechanism by which the PSA increases or decreases is associated with the cell proliferationwhich is correlating with patients age**(Hugosson et al, 2004).**

5-2 Conclusion

A significant value of PSA as cancer biomarker have issued by many researches since its approval by the US Food and Drug Administration (FDA) in 1986 , a Reference level of PSA putted was 1-4ng/ml in normal states and more than four indicates pathology. Moreover, PSA level after surgery and radical radiotherapy should be less than 0.6ng/ml for ideal treatment course and an excellent follow-up, because any variation may indicate progress of disease or recurrent.

The overall amount of PSA at time of presentation for Sudanese Prostate Cancer patients was **(87 ± 48.6 ng/ml)** and then reduced to be **(17.1±24.1ng/ml)** after Radiation therapy which in spite it was not close to reference level (less than 0.6ng/ml) after radiation and surgical operation.

The amount of patients who PSA's level was reached to acceptable normal level 1-4 ng/ml and less than 1 were 45 and 48 patients represent 23.3 percent and 24.8 per cent respectively which represents 93 of all patients treated. The majority of patients 100 patients have PSA level more than 4 represent 51.5 per cent.

A significant relation between PSA reduction and Patient age &stage , Stage 2 was dominant in the study and age group 5(64-70) years , we know that

older age have bad impact on prognosis of treatment and recovery in spite this is the common age group with prostate diseases, thus as age was younger the recovery will be good , thus PSA level will be reduced.

The interval between the surgical operation and beginning of radiotherapy in scope of the types of surgical removal had impact on PSA level, At least 1 month's interval however,partial removal was common.

The highest amount of PSA3 after radiotherapy was in age group 1 and 4(39-45.5) &(57.5-64) years 20 with level of 25and 20 ng/ml respectively. While the lowest level 3.7ng/ml in age group 2 (45.5-51.5). PSA level firstly was higher in age group 2,3 (45.5-51.5)- (51.5-57.5) years with PSA levels 108.5ng/ml for both.

There were remarkable relation between PSA level and tumor Stage, as stage increased PSA increased up to age 60 years, and later stage small reduction in PSA levels noted.

5.3 Recommendations

- The model of treatments (Partial and Total removal) and interval between those models should be assessed thus for partial removal a radiotherapy course should be accurate and the interval should be as small as possible to avoid re profilteration of cancer cell.

- There should be a spontaneously Follow up sheet included biological and chemical tests (PSA biomarker should be included) filled monthly at least which can help in evaluated the patient's condition and the treatment overcome and progression.

- Aliterature mentioned Nadir less than 1-1.2 ng/ml is favorable in early radiotherapy courseresults,consider good 1-4ng/ml also after radiation and surgery and greater than 10 after radiotherapy for late stage (3-4). Moreover any increasing above this mentioned level indicate a recurrent or metastasis of tumor.

- More sensitive technology should be used to evaluate an stander reference level for PSA in Sudan such as Monoclonal Antibody Technology

- Follow up during the first year of treatment completion is very critical aspect must be think about, which cause a problem due to absent of data for more than 2 months follow up.