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RESEARCH ARTICLE

MALIGNANT SPINAL CORD COMPRESSION, EARLY CLINICAL OUTCOME.

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Abstract

Introduction: Metastatic spinal cord compression (MSCC) is usually an oncological emergency and a well-recognized complication of cancer. Lung, prostate, multiple myeloma, non-Hodgkin lymphoma, and breast are the most common underlying tumors. These five types of malignancy, in addition to sarcomas and renal cancers account for about 70% of cases of metastatic epidural spinal cord compression. If untreated, metastatic epidural compression progresses, causing paralysis, sensory loss, and sphincter incontinence.

Material and Methods: Prospective descriptive cross sectional study to assess prognostic factors and clinical outcome of malignant spinal compression among patients attending Suez Canal university hospital in period from 2016 to 2017.

Results: A total of 48 patients were included in this study. Males accounting 45.8% and 54.2% were females. Breast cancer was the most incident (27%) to cause spinal cord compression. Dorsal vertebra was the most common site affected (45, 8%). Most of the studied patients (79.2%) presented with MSCC within less than 12 months from tumor diagnosis. 70.8% of studied population were managed by radiotherapy, 12.5% managed by surgery and 16.7% managed by both. The mean overall survival among the studied patients was 6.5 months.

Conclusions: In Egypt, no documented data of incidence of MSCC. Most of MSCC cases (79%) were presented within less than 12 months from time of primary tumor diagnosis and that was significantly related to better post management functional outcome. After management of MSCC cases 50% showed improvement of motor function, no interval changes in (41.7%) and (8.3%) showed deterioration of motor function. After 6 months of follow up of MSCC 37.5% of cases have residual and 12.5% have recurrence or progression of disease.

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Introduction:-

Metastatic spinal cord compression (MSCC) is usually an oncological emergency and a well-recognized complication of cancer (Loblaw, Laperriere et al. 2003). It can present at any time during the natural history of a

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cancer (Bucholtz, 1999) and is a major cause of morbidity in oncology patients (Husband et al, 2001). Lung, prostate, multiple myeloma, non-Hodgkin lymphoma, and breast are the most common underlying tumors. These types of malignancy, in addition to sarcomas and renal cancers, account for about 70% of cases of metastatic epidural spinal cord compression (David and Kathryn, 2011).

Metastatic spinal cord compression is defined radiographically as an epidural metastatic lesion causing true displacement of the spinal cord from its normal position in the spinal canal (Quraishi and Esler 2011).
Compression of the spinal cord or cauda equina is caused by direct tumor growth. Irreversible neurological damage ensues with resulting paraplegia. Once paraplegia develops it is usually irreversible and can affect the quality of life of the patient (Greyfriars Road, Cardiff, 2008).

The goal of treatment includes restoration of neurological status, pain relief, and prevention of further neurological damage and stabilization of the spine. When deciding the most appropriate treatment option for a patient it is important to consider quality of life issues (White, Stirling et al. 2008).
As Quinn and DeAngelis state, "Since epidural spinal cord compression is usually associated with inadequate control of the primary tumor, the goal of treatment is palliative and directed at maintaining ambulation, decreasing tumor bulk, and relieving pain. Options include symptomatic therapy, radiation, surgery, and chemotherapy (Abrahm 2004).

The aim of this study was to assess prognostic factors of malignant spinal cord compression including demographic data, pathology of primary tumor, clinical presentation, diagnosis and management and to stress on factors that can be modified for better outcome to improve quality of life of patients and increase ability of independency.

Materials and methods
This is a prospective descriptive cross sectional study .A total of 48 patients diagnosed with malignant spinal cord compression were enrolled in this study to assess prognostic factors and clinical outcome of malignant spinal compression among patients attending Suez Canal university hospital in period from 2016 to 2017.

Inclusion criteria:
All patients presented with spinal cord compression due to malignant tumors, aged ≥ 15years old.

Exclusion criteria:
Patients presented with spinal cord compression due to malignant tumors of primary spinal cord origin, patients with performance 4, patients aged ≥ 80 years old, and established paraplegic patients for more than one month.
Data were collected from patient interviewing and file records and it includes:
1- Pre management:

Demographic data:
Performance using ECOG-PS score (Oken M, et al. 1982).

Data related to disease:
Pathology of primary disease, presence of any other visceral metastasis (mets) and presence of any other affected bone. Interval between onset of disease and development of spinal cord compression, symptoms of presentation (back pain, weakness of motor function, hypothesia, urine and stool incontence), grade of motor function (we use 5-point scale : Grade 0: normal strength, Grade 1: ambulatory without aid, Grade 2: ambulatory with aid, Grade 3: not ambulatory, grade 4: paraplegia).

Data related to Management:
Interval between onset of symptoms and treatment, method of treatment either surgery, radiotherapy, or both.

Post management;
Functional outcome was rated using 5- point scale then performed with the ordered-logit model, because these data were ordinal (−1 =deterioration, 0 = no change, 1 = improvement of motor function and including assessment of motor power as follow:

1. 0= absent voluntary contraction.
2. 1=Feeble contractions that are unable to move a joint.

3. 2=Movement with gravity eliminated.
4. 3=Movement against gravity.
5. 4=Movement against partial resistance.
6. 5=Full strength. **(Nalini Vadivelu, et al. 2011).**

And sensory function as intact sensation, hypothesia, or loss of sensation, and sphincter control as preserved function or loss of control.

Local control and survival rates .Patients were followed until death or 12 months in those alive at the last follow-up visit.

1. Data collected and coded then entered as a spread sheets using Microsoft excel for windows office 2010.
2. Data were analyzed using SPSS program version 17.
3. Data were presented as tables and graphs; we used t test to compare between quantitative data that were expressed as mean and standard deviation.
4. Chi square test was used to compare between the qualitative data expressed as number and percent.
5. P value < 0.05 will be considered as significant.

Results:-

Most of the patients were less than 65 years old, and there was no sex predominance in patients, most of them had PS 1-2 (Table 1).

Table 1:-demographic data among study group:

	Frequency	**Percentage**
Age :		
Less than 65 years old	32	66.66%
More than 65 years old	16	33.33%
Sex :		
Male	23	47.9%
female	25	52.08%
Chronic illness: Yes	9	37.5%
No	15	62.5%
ECOG performance status: 1-2	15	62.5%
2-3	9	37.5%

Any type of tumor can cause malignant spinal cord compression, breast cancer was the most incident(27%) to cause spinal cord compression followed by lung cancer and multiple myeloma (16.7%), 12.5% caused by prostate cancer. Dorsal vertebra was the most common site affected (45. 8%), 20. 8% have whole spine affected. Multiple level were involved in 54. 2%. Only 42% of patients have paraspinal mass compressing the spinal cord, 25% of the studied populations have visceral mets at time of diagnosis (Table 2).

Table 2:-characteristics of tumor causing spinal cord compression

	Frequency (n)	Percentage %
Type of primary tumor		
Breast cancer	13	27%
Multiple myloma	8	16.7%
Prostate cancer	6	12.5%
Lung cancer	8	16.7%
colorectal	4	8.3%
lymphoma	2	4.2%
sarcoma	2	4.2%
metastasis of unknown origin	3	6,2%

gastro esophageal	2	4 %
Level of involved vertebra		
	4	8,3%
Cervical	22	45,83%
Dorsal vertebra	6	12,5%
Lumber vertebra	6	12,5%
Dorsolumbar vertebra	10	20,8%
Whole spine		
Number of involved vertebra		
1-2 vertebra	22	45.8%
More than 3 vertebra	26	54.2%

Presence of parasinal mass		
Yes	10	41.7%
no	14	58.3%
Presence of visceral Mets at time of diagnosis:		
Yes	6	25%
no	18	75%

Most of the compression events occurred in the first year (79.2%). 45% started management within two weeks from onset of symptoms, while 25% of cases started late after 2 weeks of symptoms presentation. Large number of patients (n=22) 45.8% of patients presented with motor deficit, 41.7% presented with back pain. At time of diagnosis, 33% of studied population were ambulatory without aid and 37.5% were not ambulatory. According to motor power at time of diagnosis, 41.7% of studied group move with gravity and 12.5% move against less resistance. However, 50% patients had intact sensation and 83.3% had content urine and stool function (Table 3).

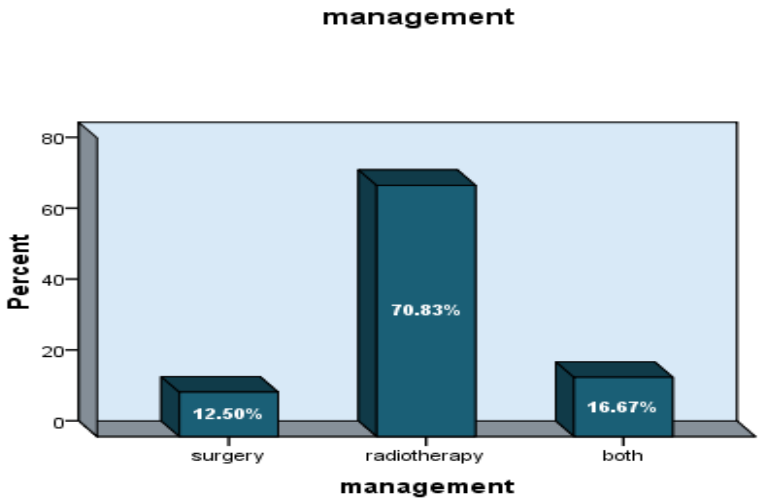
Table 3:-clinical presentation of MSCC;

	Frequency(n)	Percentage (%)
Interval from tumor diagnosis to MSCC:		
Less than 12 months	38	79.2%
More than 12 months	10	29.8%
Time developing motor deficit before management:		
1-7 days	14	29.2%
7-14 days	22	45.8%
More than 14 days	12	25%
Presentation symptoms of MSCC:		
Back pain	20	41.7%
Motor deficit	22	45.8%
Sensory deficit	2	4.2%
both	4	8.3%
Motor symptoms according to 5 point scale:		
Grade 0: normal strength	0	0%
Grade 1: ambulatory without aid	16	33.3%
Grade 2: ambulatory with aid	2	4.2%
Grade 3: not ambulatory	18	37.5%
Grade 4: paraplegic	12	25%
Presented motor power:		
No contraction or movement	6	12.5%
Trace of contraction	6	12.5%
Movement with gravity	20	41.7%
Movement against gravity	10	20.8%
Movement against less resistance	6	12.5%
Normal strength	0`	0%

Sensory function		
Intact sensation	24	50%
Hypothesia	24	50%
Loss of sensation	0	0
Urine and stool incontinence		
Yes	8	16.7%
No	40	83.3%

Radiotherapy was the most frequent first line of treatment used to treat 70.8% of studied population ,surgery was the first line of treatment for 12.5% of the patients while 16.7% managed by both (Figure 1).

Figure 1:-Type of management:



After management, functional improvement was achieved in 50% of cases, 41.7% showed no change. Assessment of motor power post management also showed that 33.3% of cases were grade 4, (29.2%) were grade 2 and (16.7% were grade 5 (normal strength) (Table 4).

Table 4:-post management outcome:

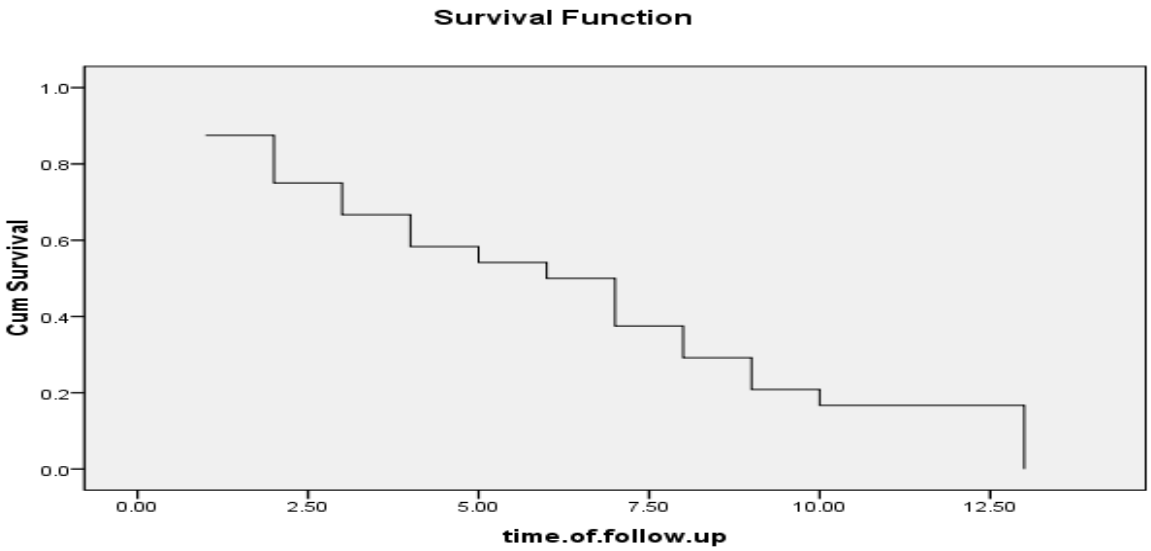
	Frequency (n)	Percentage (%)
Post management functional outcome:		
Deterioration	4	8.3%
No change	20	41.7%
Improvement of motor function	24	50%
Functional outcome grade according to 5 point scale:		
Grade 0: normal strength.	10	20.8%
Grade 1: ambulatory without aid.	6	12.5%
Grade 2: ambulatory with aid.	8	16.7%
Grade 3: not ambulatory.	14	29.2%
Grade 4: paraplegia.	10	20.8%
Motor power post management:		
Grade 0:No contraction or muscle movement	6	12.5%
Grade 1: trace of contraction	4	8.3%
Grade 2: movement with gravity	14	29.2%
Grade 3: movement against gravity	0	0%
Grade 4: movement against mild resistance	16	33.3%
Grade 5: normal strength	8	16.7%

The mean overall survival of the patients form the time of presentation was 6.5 months and 49.8% of studied population survived for 6 months or more (Table 5).

Table 5:-Overall survival form the time of MSCC:

Overall survival (months)	Number (n)	Percentage (%)
Less than 3 months	16	33.3%
3-6 months	8	16.7%
6-9 months	14	29.2%
9-12 months	10	20.8%

Figure 2:-show survival curve of studied population:



Neither the type of primary tumor, number of involved vertebrae, type of involved vertebrae, presence of Para spinal mass or presence of visceral Mets have significant effect on functional outcome among the studied population (Table 6).

Table 6:-Impact of disease related data as a potential prognostic factor on functional outcome:

	Improvement n (%)	No change n (%)	Deterioration n (%)	p
Type of primary tumor				
Breast cancer (n=10)	6	4	0	
multiple myeloma (n=10)	8	2	0	
prostate cancer (n=6)	0	6	0	
lung cancer (n= 8)	6	0	2	0.14
other tumors (n=14)	4	8	2	
No of involved vertebrae				
1-2 (n=24)	12	6	4	
3 or more (n=26)	12	14	0	0.723
Type of involved vertebrae				
cervical vertebrae (n=0)	0	0	0	
dorsal vertebrae (n=24)	14	8	2	
lumber vertebrae (n=2)	0	0	2	0.73
Dorso-lumbar vertebrae (n=8)	6	2	0	
whole spine (n=14)	4	10	0	
Presence Para spinal mass				

Yes (n=20)	10	8	2	
No (n=28)	14	12	2	0.91
Visceral Mets at the time of radiotherapy				
Yes (n= 12)	6	4	2	
No (n=36)	18	16	2	0.72

Better functional outcome was achieved when the interval between tumor diagnosis and development of MSCC was less than 12 months (p=0.021). Also early management (within one week of developing motor deficits) and motor power of patients before management has significant effect on functional outcome of MSCC (p= 0.014) and (p=0.49) post management. However, neither presentation symptoms, sensory function nor urine and stool incontinence have any significant effect on functional outcome post management (Table 7).

Table 7:-Impact of data related to presentation symptoms as a potential prognostic factor on functional outcome:

	Improvement n (%)	No change n (%)	Deterioration n (%)	p
Interval from tumor diagnosis to MSCC				
Less than 12 months (n=38)	14	20	4	
more than 12 months (n=10)	10	0	0	**0.021**
Presentations symptoms of MSCC				
back pain (n= 20)	8	10	2	
motor deficit (n= 22)	16	4	2	
sensory deficit (n= 2)	0	2	0	0.74
both (n= 4)	0	4	0	
Motor symptoms 5point scale				
grade 0: normal strength (n=0)	0	0	0	
grade 1: ambulatory without aid (n=16)	14	2	0	
grade 2: ambulatory with aid (n=2)	2	0	0	**0.049**
grade 3: not ambulatory (n=18)	2	12	4	
grade 4:paraplegia (n=12)	6	6	0	
Motor power at presentation				
0= no contraction or movement (n=6)	0	6	0	
1=trace of contraction (n=6)	6	0	0	
2= movement with gravity (n=20)	4	12	4	
3= movement against gravity (n=10)	10	0	0	0.16
4= movement against less resistance (n=6)	4	2	0	
5= normal strength (n=0)	0	0	0	
Sensory function				
intact sensation(n=20)	10	8	2	
hypothesia(n=28)	14	12	2	0.54
loss of sensation(n=0)	0	0	0	
Urine and stool incontinence				
Yes (n=8)	2	6	0	
no (n=40)	22	14	4	0.58
Time developing motor deficits before radiotherapy				
1-7 days (n=14)				
7-14 days (n=22)	10	4	0	
more than 14 days (n=12)	14	6	2	**0.014**
	0	10	2	

Type of management has no significant effect on local control or overall survival (Table 8).

Table 8:-Impact of management as prognostic factors on local control after 6 months:

	no residual or recurrence	Residual n (%)	recurrence or progression n (%)	p	Overall survival at	p

	n (%)				6months n(%)	
Management						
Surgery(n=6)	0	0	4		4	
Radiotherapy(n=34)	0	14	0		14	
Both (n=8)	0	4	2	0.4	6	0.07

Discussion:-

Metastatic spinal cord compression (MSCC) is an oncological emergency and a well-recognized complication of cancer (Loblaw, Laperriere et al. 2003). Lung, prostate, multiple myeloma, non-Hodgkin lymphoma, and breast are the most common underlying tumors (David and Kathryn, 2011).

In Egypt, no documented data of incidence of MSCC, but the liver (18.7%), bladder (12.7%), non-Hodgkin's lymphoma (11.0%) and lung, bronchus, and trachea (8.2%) are commonest sites of cancer in males. The commonest sites in females are breast (38.8%), non-Hodgkin's lymphoma (8.5%), liver (4.6%), and ovary (4.5%); all represent 56.4% of cancer in females (Ibrahim, Khaled et al. 2014).

In the current study we reviewed the prognostic factors and clinical outcome of malignant spinal compression among patients attending Suez Canal university hospital in period from2016 to 2017.

In the current study most of the patients (62.5%) had PS 1-2 and 37.5% had performance 3-4. While in study done on 175 patients with MSCC from cancer of unknown primary, 28% had performance 2 and 72% had performance 3-4 (Douglas, Huttenlocher et al. 2012).

Among studied group breast cancer was the most incident (27%) to cause spinal cord compression followed by lung cancer and multiple myeloma (16.7%), 12.5% caused by prostate cancer.

Malik Tariq Rasool, Kaneez Fatima et al found in their study that15.5 % of MSCC cases were caused by breast cancer, 12.9 % caused by myeloma, 11.6% caused by lung cancer, 10.3% caused by prostate cancer, 49% caused by others (Rasool, Fatima et al. 2016). While Bach, Larsen et al stated that 19 % of MSCC cases was caused by prostate cancer, 18% caused by lung cancer 14%caused by breast cancer, 10% caused by renal carcinoma, 4% caused by myeloma and 36% caused by others (Bach, Larsen et al. 1990).

In this study dorsal vertebra was the most common site affected (45, 8%) and 20, 8% have whole spine affected. Multiple level are involved in 54, 2%. Only 42% of patients have paraspinal mass compressing the spinal cord, 25% of the studied populations have visceral mets at time of diagnosis. In the study done by Malik Tariq Rasool, Kaneez Fatima et al ,the type of vertebrae that had been affected in studied population was dorsal (72%), lumber (27.5%),cervical(8%) (Rasool, Fatima et al. 2016).

Sarah Douglas, Stefan Huttenlocher and Amira Bajrovic stated that number of involved vertebrae was 1-2 in 31%of cases, ≥3 in 68% of cases and also revealed that 50.8% had visceral Mets, at time of diagnosis of MSCC (Douglas, Huttenlocher et al. 2012).

About eighty percent of the studied population presented with MSCC within less than 12 months from tumor diagnosis, 45% started management within 7-14 days from onset of symptoms, while 25% of cases started after 2 weeks of symptoms presentation. 45.8% of patients presented with motor deficit, 41.7% presented with back pain. At time of diagnosis, 33% of studied population were ambulatory without aid and 37.5% were not ambulatory. According to motor power at time of diagnosis in this study, 41.7% of cases had motor power grade 2(move with gravity), 20.8% had motor power grade 3 (move against resistant) and 12.5% had motor power grade 4 (move against less resistance), motor power grade1 (have trace of contraction) or grade 0(no contraction). However, 50% patients had intact sensation or hypothesia and 83.3% had content urine and stool function.

Malik Tariq Rasool, Kaneez Fatima et al stated that 40% of cases presented with MSCC at time of diagnosis, 26% presented with MSCC within less than 12 months from tumor diagnosis, 16.8% presented within 13-24 months from time of diagnosis, and also 16.8% presented within more than 2years from time of diagnosis (Rasool, Fatima et al. 2016).Another study done by Bach, Larsen et al stated that 80% of the patients had their malignancy diagnosis at the

time of SCC, although the mean period from the primary malignant diagnosis to the SCC varied considerably according to the type of the primary turnout, lung: 0.5 years, prostate: 1.7 years, kidney: 2.2 years and breast: 4.6 years (Bach, Larsen et al. 1990).

Sarah Douglas and Stefan Huttenlocher stated that 50.2% of cases started management within one week from onset of symptoms of MSCC, 49.7 % started after one week from symptoms onset (Douglas, Huttenlocher et al. 2012).
Malik Tariq Rasool, Kaneez Fatima et al stated that 79% patients presented with pain localized to the site of metastasis and only 18% of the patients presented with weakness of limbs without pain. Complete paraplegia was present in 13% of patients. Sensory loss was present in only13% and bladder involvement in 22% patients at presentation (Rasool, Fatima et al. 2016).While Sarah Douglas and Stefan Huttenlocher stated that 50.8 % of cases were not ambulatory at presentation and 49% were ambulatory (Douglas, Huttenlocher et al. 2012).

Malik Tariq Rasool, Kaneez Fatima et al stated that 41.5% of cases had motor power grade 5 at presentation, 22% had motor power grade 4, 12.9% had motor power grade 3, 6.4% had motor power grade 2 , 3.8% had motor power grade 1 and 12.9% had grade 0. (Rasool, Fatima et al. 2016)

In the current study most of the patients (70.8%) of studied population were managed by radiotherapy, 12.5% managed by surgery and 16.7% managed by both. This is similar to Malik Tariq Rasool, Kaneez Fatima et al, where radiotherapy was delivered in 62 (81%) patients. No surgery or radiation therapy treatment was delivered in 12 patients due to poor prognostic features and low performance score (Rasool, Fatima et al. 2016). Also Bach, Larsen et al stated that of the 365 treated patients, most of them (43%) received treatment in the form of radiotherapy, 31% in form of laminectomy, and 26% in form of laminectomy followed by radiotherapy (Bach, Larsen et al. 1990.)

Regarding post management outcome**,** in this study, 50% of cases developed functional improvement, 41.7% showed no change in motor function and 8.3% showed deterioration. Motor function of studied population after management were 29.2% of cases not ambulatory, 20.8% were normal strength or paraplegic, 16.7% (n=4) were ambulatory with aid and 12.5 % were ambulatory without aid. Assessment of motor power post management also showed that 33.3% of cases were grade 4, 29.2% were grade 2 and 16.5 were grade 5.

While Bach, Larsen et al stated that before treatment 38% were ambulatory, after treatment 41% and a total of 79% of the patients who were able to walk before treatment remained ambulatory, whereas only 21% of the non-ambulatory paraparetic patients and 6% of the paralytic patients regained walking ability. Patients treated with laminectomy followed by radiotherapy seemed to respond better than those treated with radiotherapy or laminectomy alone, but taking the patients pretreatment motor function into account, no significant difference was observed (Bach, Larsen et al. 1990).

Malik Tariq Rasool, Kaneez Fatima et al found in their study that of 62 patients who received radiotherapy, only 26 patients had motor improvement. An analysis of these patients revealed that there was complete recovery of power in only 13 patients and all these patients had either Grade 3 or Grade 4 power before treatment. A maximum net gain of motor function was three grades of power and was found in 2 patients. No patient with Grade 0 or 1 power fully recovered. There was no improvement in 8 patients and deterioration was recorded in 3 patients. Thus, grade of power before treatment was predictive of response to treatment and overall outcome of motor or sensory functions. Delay of treatment by more than 10 days was associated with poor outcome in neurological function (Rasool, Fatima et al. 2016).

The mean overall survival among the studied population was 6.5 months and 49.8% of studied population survived for 6 months or more.

The median survival of the whole group after the diagnosis of spinal cord compression was 3.6 months and one year survival probability was 20.9%in study done by Helweg-Larsen, Sørensen et al(Helweg-Larsen, Sørensen et al. 2000). Also Sarah Douglas and Stefan Huttenlocher stated that the median survival time was 4 months (Douglas, Huttenlocher et al. 2012)

In this study, improvement of functional outcome was significantly associated with the interval between tumor diagnosis and development of MSCC less than 12 months (p=0.021), early management (within one week of developing motor deficits) (p= 0.014) and Motor power of patients before management (p=0.49).

Also Susannehelweg-Larsen, Persoelberg and Svend Kreiner state that there was a significant association (p = 0.016) between the time interval from the diagnosis of the primary tumor until the development of spinal cord compression and the gait function. Also sensory disturbances at time of diagnosis had a direct prognostic importance regarding the final gait function (p = 0.01) (Helweg-Larsen, Sørensen et al. 2000).

In our study, Local control after 6 months is significantly affected by presence of visceral mets at time of management (p= 0.031), pre management motor symptoms (p=0.036), pre-management motor power (p=0.018), and interruption of radiotherapy schedule (p=0.04).

Conclusion:-

Any type of tumor can cause malignant spinal cord compression; breast cancer was the most incident. Absence of chronic illness and good performance status (1-2) at time of presentation is significantly related to better post management functional outcome. Neither the type of primary tumor, number of involved vertebrae, type of involved vertebrae, presence of Para spinal mass or presence of visceral mets have significant effect on functional outcome among the studied population. Early management (within one week of developing motor deficits) has significant effect on functional outcome of MSCC (p= 0.014). Motor power of patients before management has significant impact on functional outcome post management. The mean overall survival among the studied patients was 6.5 months.

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