CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1288746

Available online at: http://www.iajps.com Research Article

AN OBSERVATIONAL PROSPECTIVE RESEARCH ON THE PREDICTIVE FACTORS, TRANS ARTERIAL CHEMOEMBOLIZATION WITH ASSOCIATED ADVERSE EVETS OF HEPATOCELLULAR CARCINOMA

[1]Dr. Malik Muhammad Haseeb Aslam, [2]Dr. Sidra Habib, [3]Dr. Sidra Choaudhary

[1]House Officer, Allied Hospital, Faisalabad

[2]Rawalpindi Medical College

[3]WMO Tehsil Head Quarter Ahmad Pur Sial

Abstract:

Objective: *The objective of this research was the documentation of the adverse effects of the prediction of the factors and trans arterial chemoembolization.*

Methods: *Our research was observational prospective held at Urology Department, Allied Hospital, Faisalabad (Nov, 2016 to Nov, 2017). We studied the hepatocellular carcinoma patients who developed related complications in the first six weeks of the procedure and documented every detail. Data analysis was made on SPSS software.*

Results: *Research sample included eighty patients with 59 males (73.8%) and remaining female with an age bracket of 28 – 76 years (Mean age as 52.25 ± 9.24) years. Hepatitis C was the common etiology with associated fifty-five cases of cirrhosis (68.8%), 46 adverse effects cases (57.5%), 37 cases of post trans arterial chemoembolization syndrome (46.3%). No additional complications were observed in 24 syndrome cases (64.8%); whereas, 3 renal dysfunction cases (8%), 2 hypertensive crises (5%) and one case of urinary tract infection (UTI) (2.7%), sepsis and pneumonia. Six cases of cirrhosis decompensation (7.5%) among those three died because of sepsis (50%). There was an association of the syndrome with the tumor size (above 5 cm, P-value = 0.001) and higher lipiodol dose P-value as 0.0001. Cirrhosis decompensation was linked with the low basal albumin, an advanced basal child Turcotte Pugh and end-stage liver disease model with respective (P-value = 0.002), (P-value = 0.005) and (P-value = 0.006).*

Conclusion: *Trans arterial chemoembolization is generally considered as safe but it may also lead into advanced liver disease complications as well. There is an association of the post-procedure syndrome with the increased size of the tumor and dose of the lipiodol.*

Keywords: *Hepatocellular carcinoma, Post TACE Syndrome, Lipiodol, Tumor, Syndrome and Adverse events.*

Corresponding author:

Dr. Malik Muhammad Haseeb Aslam,

House Officer, Allied Hospital,

Faisalabad

QR code

Please cite this article in press Malik Muhammad Haseeb Aslam et al., ***An Observational Prospective Research on the Predictive Factors, Trans Arterial Chemoembolization with Associated Adverse Evets of Hepatocellular Carcinoma,*** *Indo Am. J. P. Sci, 2018; 05(06).*

INTRODUCTION:

Cancer is commonly caused because of the HCC (hepatocellular carcinoma) that brings mortality all over the globe [1]. Numerous modalities which include TACE (trans arterial chemoembolization) are present to manage the incident of HCC [2]. TACE may depended on the management stage of HCC which shows a trend of HCC survival in the patients [3].

Commonly observed adverse events are fever, nausea, abdominal pain, vomiting, elevated liver enzymes (may sustain from few hours to few days) and leukocytosis including cirrhosis as vital complication [1, 4]. Treatment complications also include renal and hepatic failure causing morbidity [5, 6]. Embellishing agents and Chemotherapeutic use may also cause an acute cholecystitis, pancreatitis, biliary tract necrosis, ulcers or gastric erosions in an inadvertent injection in the organs [7 – 10]. There are few more related adverse events such as necrotic tumor infection presented in the shape of tumor lysis syndrome and liver abscess [11, 12].

There are numerous risk factors associated with the complications which include liver disease, Child Turcotte Pugh (CTP) and end-stage liver disease model [13]. The objective of this research was the documentation of the adverse effects of the prediction of the factors and trans arterial chemoembolization.

PATIENTS AND METHODS:

Our research was observational prospective held at Urology Department, Allied Hospital, Faisalabad (Nov, 2016 to Nov, 2017). We studied the hepatocellular carcinoma patients who developed related complications in the first six weeks of the procedure and documented every detail. Data analysis was made on SPSS software. We documented every related and non-related TACE adverse event. We did not include any case who had a history of radio frequency ablation in the last six month and a score of CTP over ten or HCC surgical liver resection case.

The distribution of the response was taken as 50%, CI as 95% and error margin as 5%, sample population of eighty patients was selected through "Raosoft" sample calculator.

Chemotherapeutic injection was involved in the patients with an agent (doxorubicin) which was mixed with lipiodol in the catheterized arteries which feed the tumor also followed by gel foam particles injection for the reinforcement of treatment in Radiology Dept.

We observed laboratory and clinical parameters before and after TACE on day of presentation, first, second, fifth, seventh, fourteenth, twenty-eighth, thirty-sixth and forty-second day. Detailed parameters, complications and etiology was observed as mentioned earlier. PTS was referred to fever, white cells rise, abdominal pain and occurrence of transaminases after the procedure of TACE. Cirrhosis Decompensation can be referred to the development of variceal bleeding, ascites or portosystemic encephalopathy after TACE procedure. Data was analyzed on SPSS software with a significant P-value of (< 0.05).

RESULTS:

Research sample included eighty patients with 59 males (73.8%) and remaining female with an age bracket of 28 – 76 years (Mean age as 52.25 ± 9.24) years. Hepatitis C was the common etiology with associated fifty-five cases of cirrhosis (68.8%), 46 adverse effects cases (57.5%), 37 cases of post trans arterial chemoembolization syndrome (46.3%). No additional complications were observed in 24 syndrome cases (64.8%); whereas, 3 renal dysfunction cases (8%), 2 hypertensive crises (5%) and one case of urinary tract infection (UTI) (2.7%), sepsis and pneumonia. Six cases of cirrhosis decompensation (7.5%) among those three died because of sepsis (50%). There was an association of the syndrome with the tumor size (above 5 cm, P-value = 0.001) and higher lipiodol dose P-value as 0.0001. Cirrhosis decompensation was linked with the low basal albumin, an advanced basal child Turcotte Pugh and end-stage liver disease model with respective (P-value = 0.002), (P-value = 0.005) and (P-value = 0.006). Table I, II, III and IV respectively show detailed outcomes of before TACE adverse events trend in percentage and number, PTS predictive factors (with respect to PTS and No PTS), PTS follow-up parameters and cirrhosis decompensation after TACE predictive factors.

Table – I: Post TACE Adverse Events

Adverse Events Types	Number	Percentage
Post TACE Syndrome	37	57.8
Cirrhosis Decompensation	6	9.3
Infections	6	9.3
Renal Dysfunction	3	4.7
Hypertensive Crisis	3	4.7
Isolated Abdominal Pain	2	3.1
Isolated Fever	2	3.1
Melena	1	1.6
Hematoma	1	1.6
Deaths	3	4.7
Total	64	100

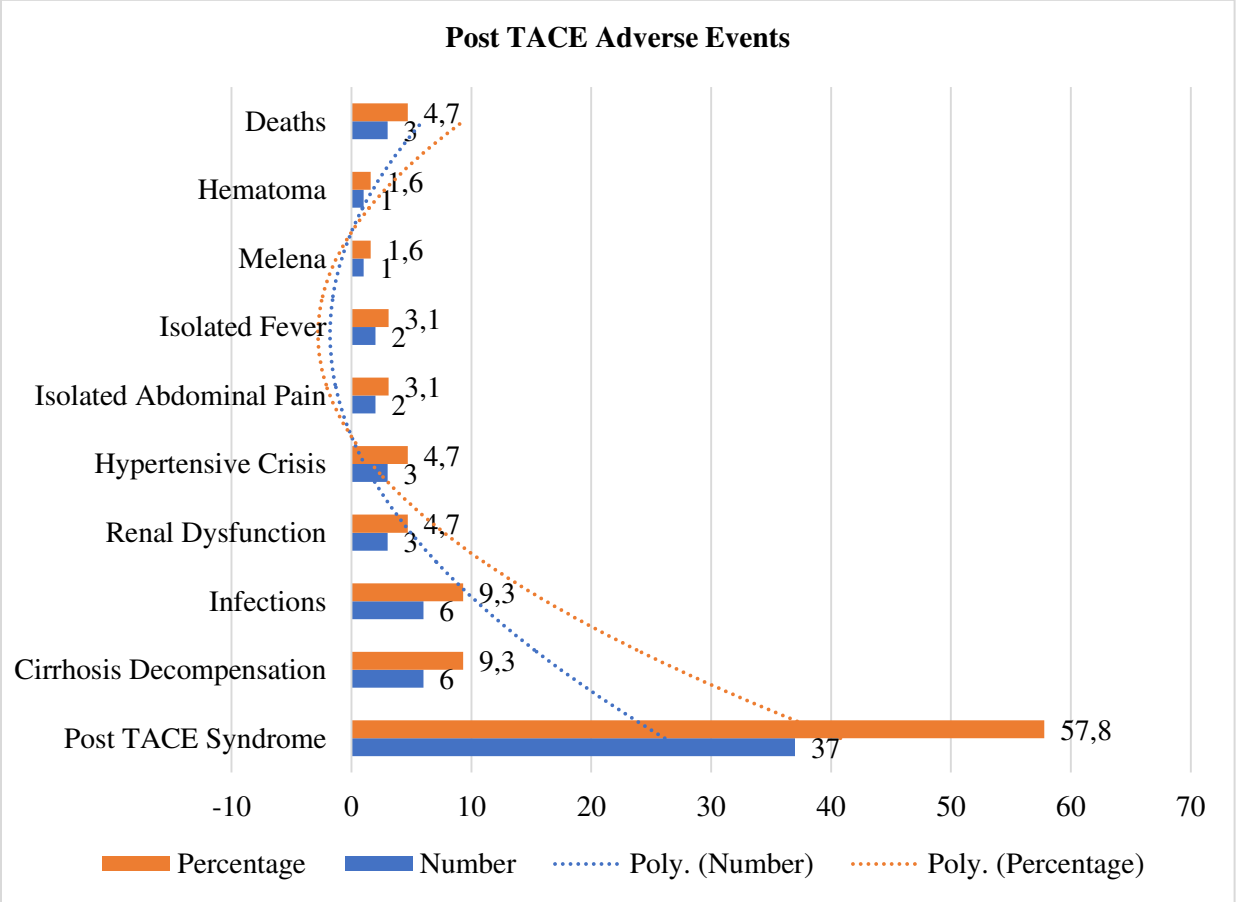


Table – II: Predictive factors of Post-TACE Syndrome (PTS).

Clinical Features		PTS	No PTS	P-value
Age	**Young**	4	2	0.407
	Middle aged to elderly	33	41	
Gender	**Male**	29	30	0.45
	Female	8	13	
Co-morbid	**Present**	17	21	0.826
	Absent	20	22	
Size of tumor	**<5cm**	8	29	0.001*
	>5cm	25	18	
Dose of Lipiodol	**<10 ml**	21	40	0.0001*
	>10 ml	16	3	
Basal platelet count	**< 100,000/mm3**	11	22	0.069
	> 100,000/mm3	26	21	
Basal PT INR	**< 1.4**	27	26	0.343
	> 1.4	10	17	
Basal SGPT (ALT)	**< 50 U/L**	23	22	0.371
	> 50 U/L	14	21	
Basal SGOT (AST)	**< 50 U/L**	13	15	1
	> 50 U/L	24	28	
Basal Albumin	**< 2.8gm/dl**	16	15	0.495
	> 2.8gm/dl	21	28	
Basal Sodium	**≤ 133 meq/L**	7	12	0.433
	> 133 meq/L	30	31	
Basal Creatinine	**< 1.2mg/dl**	30	40	0.174
	> 1.2mg/dl	7	3	
AFP	**< 200 ng/ml**	24	29	0.817
	> 200 ng/ml	13	14	
Basal CTP score	**CTP A**	22	23	0.655
	CTP B/C	15	20	
Basal MELD score	**< 10**	22	22	0.505
	> 10	15	21	

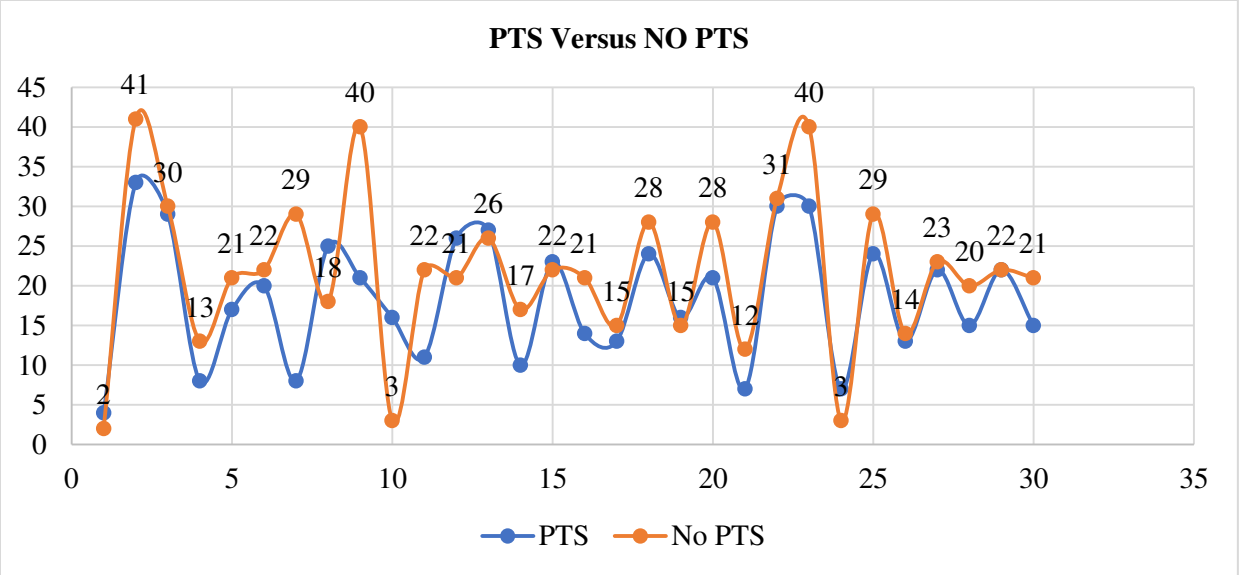


Table – III: Follow up parameters in patients with Post-TACE Syndrome (PTS).

Clinical Features		PTS	No PTS	P-Value
Rise in Temperature	**> 1010 F**	33	13	0.000*
	< 1010 F	4	30	
Abdominal pain	**Yes**	31	10	0.000*
	No	6	33	
Rise in WBC	**< 3000/mm3**	8	34	0.000*
	> 3000/mm3	29	9	
Rise in Total bilirubin	**< 1mg/dl**	9	30	0.000*
	> 1mg/dl	28	13	
Rise in SGPT (ALT)	**<200 U/L**	14	39	0.000*
	>200 U/L	23	4	
Rise in SGOT (AST)	**<200 U/L**	10	37	0.000*
	>200 U/L	27	6	
Rise in PT INR	**> 3sec**	15	10	0.146
	< 3sec	22	33	
Rise in Creatinine	**> 1mg/dl**	6	1	0.045*
	< 1mg/dl	31	42	
Rise in CTP score	**≥ 2**	8	2	0.038*
	< 2	29	41	
Rise in MELD score	**≥ 2**	26	15	0.002*
	< 2	11	28	
Decompensation	**Yes**	5	1	0.09
	No	32	42	
Death	**Yes**	3	0	0.095
	No	34	43	

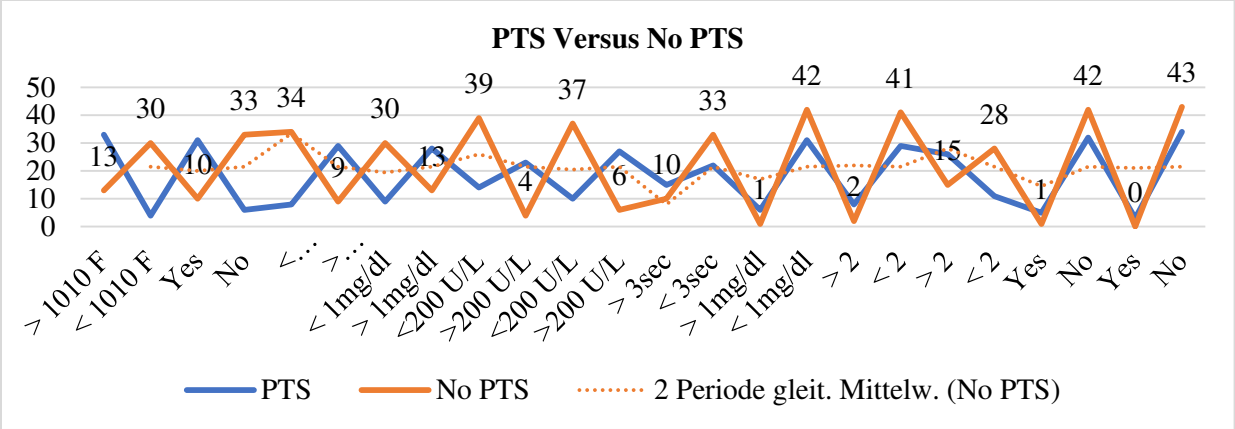
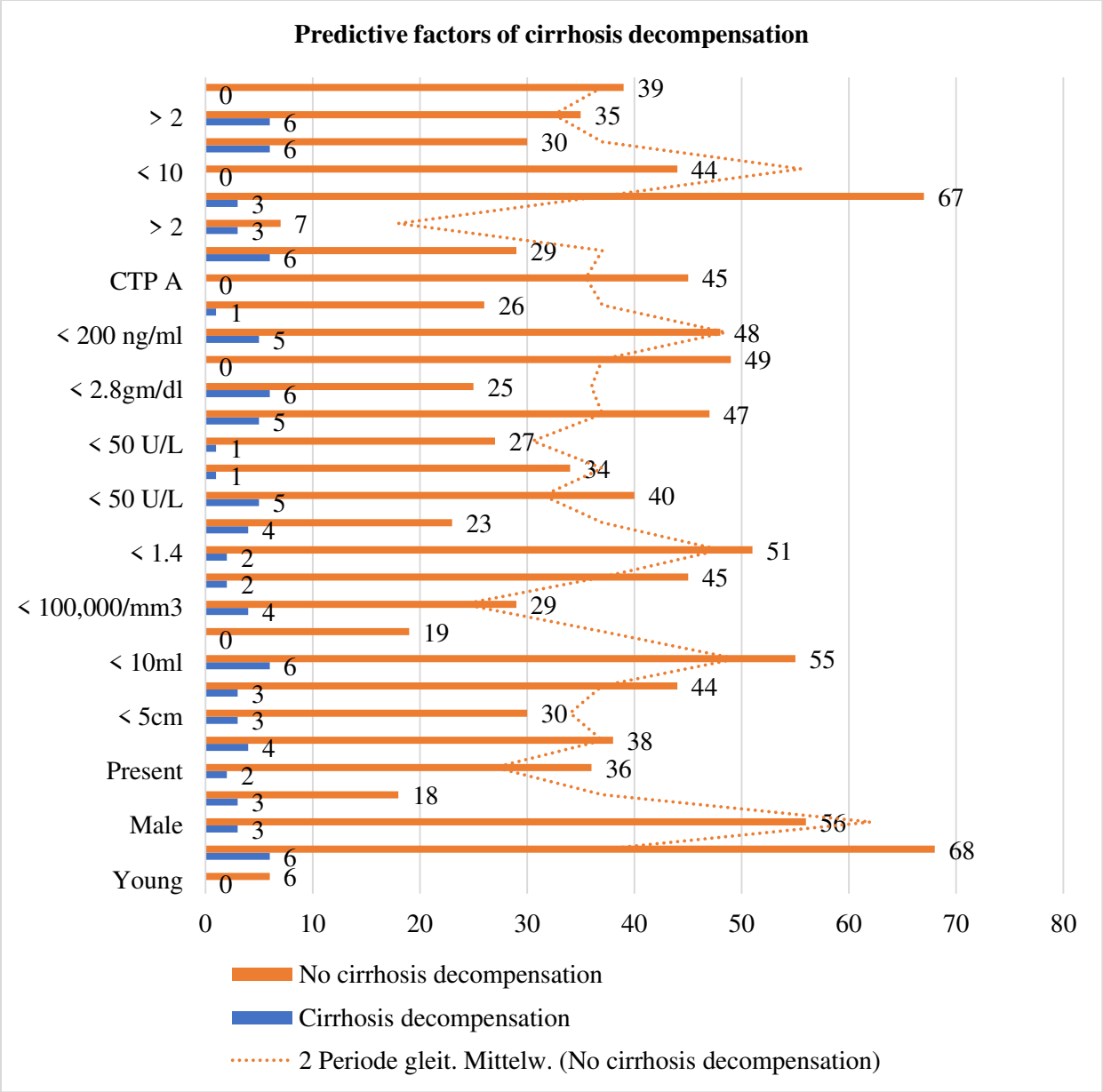


Table – IV: Predictive factors of cirrhosis decompensation following TACE

Clinical Features		Cirrhosis decompensation	No cirrhosis decompensation	P-Value
Age	**Young**	0	6	1
	Middle aged to elderly	6	68	
Sex	**Male**	3	56	0.182
	Female	3	18	
Comorbid	**Present**	2	36	0.678
	Absent	4	38	
Size of tumor	**< 5cm**	3	30	0.687
	> 5cm	3	44	
Dose of Lipiodol	**< 10ml**	6	55	0.327
	> 10ml	0	19	
Basal platelet count	**< 100,000/mm3**	4	29	0.224
	> 100,000/mm3	2	45	
Basal PT INR	**< 1.4**	2	51	0.172
	> 1.4	4	23	
Basal SGPT (ALT)	**< 50 U/L**	5	40	0.223
	>50 U/L	1	34	
Basal SGOT (AST)	**< 50 U/L**	1	27	0.659
	> 50 U/L	5	47	
Basal Albumin	**< 2.8gm/dl**	6	25	0.002*
	> 2.8gm/dl	0	49	
AFP	**< 200 ng/ml**	5	48	0.658
	< 200 ng/ml	1	26	
Basal CTP score	**CTP A**	0	45	0.005*
	CTP B/C	6	29	
Rise in CTP score	**≥ 2**	3	7	0.024*
	< 2	3	67	
Basal MELD score	**< 10**	0	44	0.006*
	> 10	6	30	
Rise in MELD score	**≥ 2**	6	35	0.026*
	< 2	0	39	



DISCUSSION:

Various adverse events after TACE and predictive factors have been assessed in this particular research as few side effects have been already mentioned in earlier publications [14 – 16]. According to a European author one acute liver failure episode was experienced by the patients within short duration of TACE (60%) [17]. Contrary to that a research was carried out in Hong Kong which reports liver failure incidence as (1.5%) in the sample population of 132 [18].

PTS associated symptoms have been also reported as observed in this particular research with same occurrence frequency and time [4]. There is a symptomatic treatment of the syndrome which is self-limited as number of cases showed a decrease in the severity and we also observed PTS as common symptom.

Variables outcomes have been reported in numerous research studies as one author relates TACE complications with HCC patients, bilirubin increase after TACE and linked with the cirrhosis stage and chemotherapeutic agent dose the association of PTS was made with chemotherapeutic agent dose; whereas, not with the cirrhosis stage as shown by basal CTP score.

There was a close relation of the cirrhosis decompensation with liver disease stage which was

reflected by level of basal albumin and basal CTP score as observed in this particular research. Relation of the TACE severe complication was established with portal hypertension and poor hepatic function and with reflux and overdose of chemotherapeutic agents by another author [19]. It can be concluded that there may be a prevention of the associated complications with a closed supervision, protection and observation of the hepatic function.

Our research observed TACE complications as septic anemia that was a reason of three patient's death two (advanced liver disease) and one Class C case because of the immunosuppression. The incidence of cirrhosis decompensation was also established in the other research studies at advanced liver disease stage [19].

Fever after TACE because of tumor size and chemoembolization dosage was a reason of HCC after TACE as observed in a research held in Taiwan [20]. There was also a relation of the PTS with the tumor size and chemotherapeutic agent dose. In a Korean research acute hepatic failure risks after transcatheter arterial HCC chemoembolization were also established [5]. There was no separate dealing of acute hepatic failure in this research as TACE abuse is the case of an acute chronic injury that leads to cirrhosis decomposition or PTS. The outcomes TACE as decompensation were observed in 7.5% patents without any relation with the PVT as P-value was considered (1.00). The patients with no partial PVT & not those having main PVT were selected. Wisconsin (USA) is of the view that chemoembolization in the high-risk patients was observed for complications and outcomes [21]. It can be summarized that advanced disease patients and decreased hepatic reserve cases managed with TACE display no enhancement in the mortality and morbidity with no survival decrease. The performance of TACE is safe in the relative risk factors cases which may be categorized in the group with high risk factor involvement. As we observed that 42.5 percent cases were without complications and three advanced liver disease deaths. There was a significant relation between an advanced MELD and CTP scores and cirrhosis decompensation progression. Hence, TACE cases need careful selection because numerous complications were seen in the two weeks duration after TACE. Our research concludes that close supervision is mandatory for a duration and PTS time period that is to be decreased to 2 weeks. Moreover, due to significant MELD score decrease in the cases who progressed in PTS, MELD increase is suggested which may be made a part of the PTS definition.

CONCLUSION:

Trans arterial chemoembolization is generally considered as safe but it may also lead into advanced liver disease complications as well. There is an association of the post-procedure syndrome with the increased size of the tumor and dose of the lipiodol.

REFERENCES:

1. Bruix J, Castells A, Montanya X. Phase II study of trans arterial embolization in European patients with hepatocellular carcinoma: need for controlled trials. Hepatology 1994; 20: 643-50.
2. Groupe d'Etude et de treatment du carcinoma hepatocellular. A comparison of lipiodol chemoembolization and conservative treatment for unresectable hepatocellular carcinoma. N Eng J Med 1995; 11: 1256-61.
3. Ngan H, Lai CL, Fan ST, Lai EC, Yuen WK, Tso WK. Transcatheter arterial chemoembolization in inoperable hepatocellular carcinoma: four-year follow up. J Vascu Interv Radiol 1996; 7: 419-25.
4. Liang SN, Liu LL, Su HY, Feng B, Zhao GS, Xu K. Analysis of severe complications after transcatheter arterial chemoembolization for primary hepatocellular carcinoma. Zhonghua Zhong Liu Za Zhi2008; 30: 790-2.
5. Li CP, Chao Y, Chen LT, Lee RC, Lee WP, Yuan JN, et al. Fever after transcatheter arterial chemoembolization for hepatocellular carcinoma: incidence and risk factor analysis. Scand J Gastroenterol 2008; 43: 992-9.
6. Kiely JM, Rilling WS, Touzios JG, Hieb RA. Chemoembolization inpatients at high risk: results and complications. J Vasc Interv Radiol 2006; 17: 47-53.
7. Huo TI, Wu JC, Lee PC, Chang FY, Lee SD. Incidence and risk factorsfor acute renal failure in patients with hepatocellular carcinoma undergoing trans arterial chemoembolization: a prospective study. Liver Int 2004, 24: 210-5.
8. Wagnetz U, Jaskolka J, Yang P, Jhaveri KS. Acute ischemic cholecystitis after trans arterial chemoembolization of hepatocellular carcinoma: incidence and clinical outcome. J Comput Assist Tomogr 2010; 34: 348-53.
9. Kim HK, Chung YH, Song BC, Yang SH, Yoon HK, Yu E, et al. Ischemic bile duct injury as a serious complication after trans arterial chemoembolization in patients with hepatocellular carcinoma. J Clin Gastroenterol 2001, 32: 423-7.
10. Beyza Özç?nar, Koray Güven, Arzu Poyanl?, Ilg?n Özden. Necrotizing pancreatitis after transcatheter arterial chemoembolization for

hepatocellular carcinoma. Diagn Interv Radiol 2009, 15: 36-8.
11. Hirakawa M, Iida M, Aoyagi K, Matsui T, Akagi K, Fujishima M. Gastroduodenal lesions after transcatheter arterial chemoembolization in patients with hepatocellular carcinoma. Am J Gastroenterol 1988; 83: 837-40.
12. Vander Walde A, Marx H, Leong L. Liver Abscess as a Complication of Hepatic Trans arterial Chemoembolization: A Case Report, Literature Review, and Clinical Recommendations. Gastrointest Cancer Res 2009; 3: 247-51.
13. Hsieh PM, Hung KC, Chen YS. Tumor lysis syndrome after trans arterial chemoembolization of hepatocellular carcinoma: case reports and literature review. World J Gastroenterol 2009; 15: 4726-8.
14. Chung J W, Park J H, Han J K. Hepatic tumors: predisposing factors for complications of transcatheter oily chemoembolization. Radiology 1996; 198: 33-40.
15. Sasaki Y, Imaoka S, Kasugai H. A new approach to chemoembolization therapy for hepatoma using ethiodized oil, cisplatin, and gelatin sponge. Cancer 1987; 60: 1194-203.
16. Venook AP, Stagg RJ, Lewis BJ. Chemoembolization for hepatocellular carcinoma. J Clin Oncol 1990, 8: 1108-14.
17. Chan AO, Yuen MF, Hui CK, Tso WK, Lai CL. A prospective study regarding the complications of transcatheter intraarterial lipiodol chemoembolization in patients with hepatocellular carcinoma. Cancer 2002; 94: 1747-52.
18. Caturelli E, Siena DA, Fusilli S. Transcatheter arterial chemoembolization for hepatocellular carcinoma in patients with cirrhosis: evaluation of damage to nontumorous liver tissue – long-term prospective study. Radiology 2000; 215: 123-8.
19. Josep M, Llovet J B. Systematic review of randomized trials for unresectable hepatocellular carcinoma: Chemoembolization improves survival. Hepatology 2003; 37: 429-42.
20. Leung DA, Goin JE, Sickles C, Raskay BJ, Soulen MC. Determinants of postembolization syndrome after hepatic chemoembolization's Interv Radiol 2001; 12: 321-6.
21. Jeon SH, Park KS, Kim YH, Shin YS, Kang MK, Jang BK, et al. Incidence and risk factors of acute hepatic failure after transcatheter arterial chemoembolization for hepatocellular carcinoma. Korean J Gastroenterol 2007; 50: 176-82.