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Association of p53 Gene Polymorphism with Functional Outcome among Traumatic Brain Injury patients: A Cohort Study

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Abstract

Introduction: Traumatic brain injury is one of the leading cause of mortality. The guardian of genome p53 and polymorphism of this gene has been least studied in TBI. Evaluation of the patterns of Arg 72 Pro polymorphism of p53 gene in TBI patients as compared to controls as well as to evaluate the association of p53 gene polymorphisms with the functional outcome of TBI were the objectives of this study.

Methods: The influence of the Arginine variant of p53 was investigated in a cohort of 58 adults with mild, moderate, and severe TBI with PCR-RFLP method.The neuropsychiatric outcomes of the patients were assessed after 3 and 6 months of injury using the following questionnaires; (i) Extended Glasgow Outcome Scale (GOSE)- measure global functioning (ii) Rivermead Head Injury Follow-up Questionnaire (RHFUQ) an index of psychosocial outcome; (iii)Quality of Life after Brain Injury-Overall Scale (QOLIBRI-OS) an index of health-related quality of life after brain injury.

Results: No significant difference was observed between the allelic distribution of genotype variants among cases and controls. *T*he mean value of GCS was highest in patients with CC genotype. The highest GOSE score was observed in proline containing genotype (CC), suggesting a better outcome. Among all the outcome tools used, RFHUQ3 was the most sensitive (85.7%) and specific (90%) with a cut-off value of 6.5. The area under the curve (AUC) was the highest for RFHUQ at 3 months (0.958).

Conclusion: There was no significant association between p53 gene polymorphism and functional outcome after TBI. However, patients with CC genotype (proline/proline) had less severe injuries, whereas the extent of recovery was maximum in GG-containing genotypes, supported by their longest length of hospital stay. RHFUQ was the most sensitive and specific tool to assess the functional outcome after TBI when GOSE is the gold standard.

Keywords: p53, gene polymorphism, Traumatic Brain Injury, Arginine variant, proline variant, functional outcome.

I. BACKGROUND

Traumatic brain injury (TBI) is one of the most common causes of disability and mortality worldwide. Apoptosis occurs in neurons and glia after TBI, according to studies, and may contribute to neurological dysfunction[1,2]. Apoptotic cell death has been linked to

decreased expression of survival-promoting proteins like Bcl-2 and extracellular signal-regulated kinase and increased expression of death-inducing proteins including Bax, c-Jun N-terminal kinase, p53, calpain, and caspases following TBI [1,3]. DNA repair, cell cycle progression, apoptosis, and neural damage are all regulated by the p53 tumour suppressor factor [4]. Shortly after TBI, p53 is activated, and inhibiting it is thought to provide neuroprotection [5,6].

In a study consisting a group of 90 severely head-injured patients hospitalised to an intensive care unit, a functional polymorphism of the p53 gene in codon 72 which modifies the characteristics of the produced protein was explored[7]. At the time of discharge, 78 patients with the Arg/Arg genotype had an unsatisfactory result. However, no significant difference was identified 6 months later between the groups of patients with and without the Arg/Arg genotype, suggesting that p53 may only play a minor role in the long-term clinical prognosis of individuals who have sustained TBI.

There have been very few studies in the literature that have investigates the relationship between genes and their polymorphisms and the outcome of severe traumatic brain damage. P53 is one such gene that has received little attention in TBI. A study like this will provide new insights into the therapy options for TBI. The link between these genes and their polymorphisms and TBI outcomes could serve as a foundation for future treatment trials targeting these genes. This will usher in a whole new era of genetic therapy methods for TBI treatment. Gene polymorphism could be an early indicator of how severe TBI will affect a person's outcome. To the best of our knowledge, there are only a handful such studies available.

The Glasgow Outcome Scale (GOS) was employed in the majority of research as a primary outcome measure for therapies in traumatic brain injury patients. However, GOS has a flaw in that it lacks the sensitivity to detect tiny but clinically significant changes in TBI outcome. The Glasgow Outcome Scale-Extended (GOSE) may be able to help with this.

GOSE is a global scale for the functional outcome that rates patient status into eight categories, dead, vegetative state, severe disability upper and lower, moderate disability upper and lower, and good recovery, both upper and lower.In comparison to the Glasgow outcome scale, which was used as a gold standard tool to assess the outcome in our study, the extended Glasgow outcome scale (GOSE) is a more sensitive and preferred tool.

The Rivermead head injury follow-up questionnaire (RHFUQ) is a short, easy, adequate reliable, and valid assessment of outcome that can be used across the severity spectrum, but especially after mild to severe head injuries.

The QOLIBRI-OS (Quality of Life after Brain Injury- Overall Scale) is a new health-related quality-of-life (HRQoL) tool designed exclusively for those who have had a traumatic brain injury (TBI). It includes a six-domain HRQoL profile as well as an overall score.

The study intends to explore the functional outcome, in terms of GOSE, RHFUQ, and QOLIBRI-OS after TBI as well as its association with p53 gene polymorphism.

Objectives

The objectives of the study were to,

1. evaluate the patterns of Arg 72 Pro polymorphism of p53 gene in TBI patients as compared to controls
2. find out whether there is an association of p53 gene polymorphisms with the outcome after traumatic brain injury, in terms of the functional outcome as assessed by extended Glasgow outcome scale(GOSE), Rivermead head injury service follow up questionnaire (RHFUQ), and quality of life after brain injury (QOLIBRI-OS) .

II. METHODOLOGY

The present cohort study was conducted in the Department of Biochemistry in the Molecular division of Central Research Laboratory in

collaboration with the Department of Neurosurgery, KSHEMA, Mangalore,India.

Inclusion Criteria

TBI patients with mild, moderate, and severe injury after resuscitation and stabilization at admission, between the age group of 18-60 years were recruited. University ethics committee approval was sought before starting the study.

Exclusion Criteria

TBI patients with anoxic intra-cerebral damage or brain death, spinal cord injury, neurological disorders, or cerebrovascular diseases were excluded.

Sample collection and analysis

After receiving written informed consent from the patient or their first-degree relatives, three mL EDTA whole blood was obtained and genotyping was performed. The salting-out approach was used to isolate DNA. Electrophoresis on a 0.8 percent agarose gel with ethidium bromide (0.5 g/ml) in TAE buffer was used to verify the DNA quality. The spectrophotometer was used to assess the quantification and purity of DNA (OD260 / OD280 ratio).

Amplification and Genotyping of the gene polymorphism:

Genotyping of the p53 gene was carried out by PCR-RFLP. Details of forward and reverse primers, restriction enzymes, and reaction conditions are as depicted in table 1.

Table 1: *PCR-RFLP Reaction Conditions for the genotyping of p53*

SNP	Location (Base change)	Forward Primer Reverse Primer	PCR Program (35 cycles)	PCR Fragment length (Bp)	Restriction enzyme, Incubation temperature	Allele: RFLP fragment size
p53 Arg72Pro (rs1042522)	Promoter G>C Arg>Pro	5’ CCTGAAAACA ACGTTCTGGT AA 3’ 5’ GCATTGAAGC TCCATGGAAG 3’	94°C, 5” 94°C,30’, 55°C,30’, 72°C,30’ 72°C, 7”	448bp	BstUI, 37°C	248 bp

Outcome assessment:

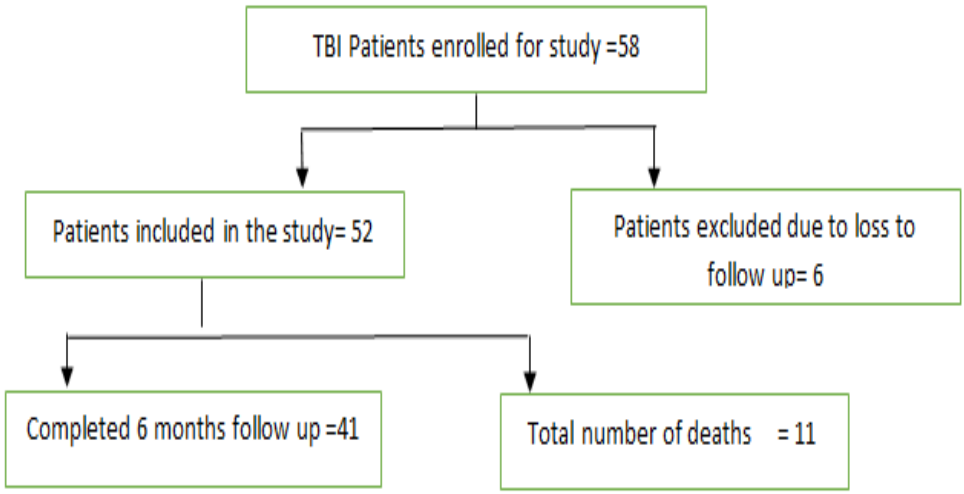

Figure 1: *Flowchart depicting patients included in the study.*

Functional outcome after TBI was carried out using Outcome tools like Rivermead head injury service follow-up questionnaire (RHFUQ), quality of life after brain injury (QOLBRI-OS), and extended Glasgow outcome scale (GOSE). Outcome assessment was done at three months and six months following injury.

Statistical analysis:

Statistical analysis was carried out using the software, Graphpad Instat version 3. Hardy Weinberg Equilibrium (HWE) was carried out to evaluate the allelic distribution and the $\chi 2$ test was used to assess the association between genetic polymorphism and outcome. Kruskal Wallis followed by the post hoc test, Dunn's test was carried out to compare functional outcomes between different allelic variants as well as to compare the scores at admission, discharge, 3 months, and 6 months. Mann Whitney U test was carried out to compare the scores at 3 months and 6 months within the group. Receiver operative characteristic curves(ROCs) were constructed to compare the utility of outcome tools. Spearman's correlation coefficient was calculated for the correlation between length of stay and functional scores of GOSE, RHFUQ, and QOLIBRI-OS.

III. RESULTS

Fifty-eight TBI cases with a mean age of 38.66± 12.2 (17,62) years and fifty-eight controls with the mean age of 34.3± 12.87 (21,60) years were the study participants. The ratio of males to females was 3:1 in cases and 4:1 in controls. The causes of injury were mainly road traffic accidents (RTA) (71.4%) and falls (26.19%), assault, and other (2.41%).

Polymerase Chain Reaction and Restriction Fragment Length Polymorphism was carried and digested fragments were visualized on Gel electrophoresis using 2% Agarose gel (Table 1). Fragments which are undigested (448bp) are CC, fragments with 248 bp are GG and CG are marked by both 448bp and 248bp bands (Figure 3).

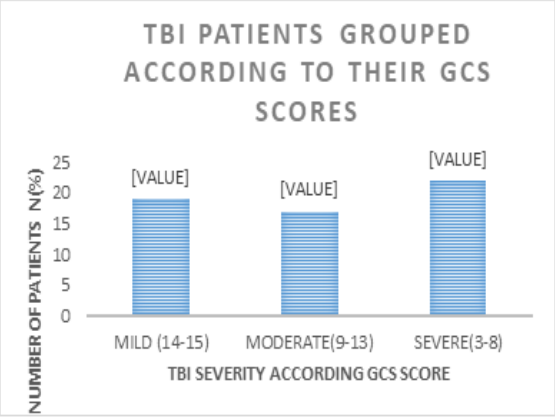

Figure 2: *Showing grouping of TBI patients according to their GCS score on admission.*

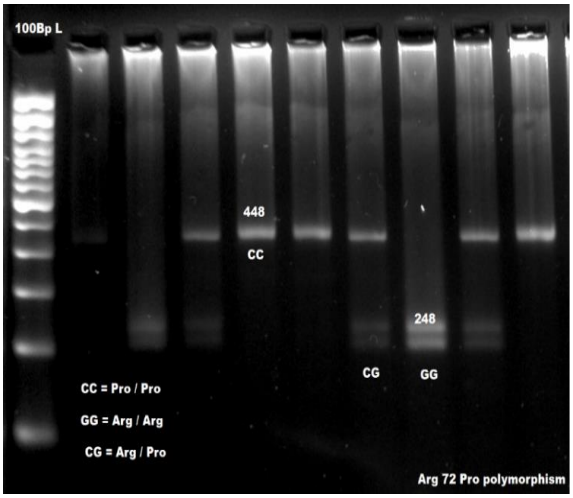

Figure 3: *Agarose gel electrophoresis of RFLP digested p53 PCR with BstU1 restriction enzyme.*

There was no significant difference was observed between the allelic distribution of genotypes, homozygous dominant (GG) (wild), heterozygous (CG), and homozygous recessive (CC) (mutant) alleles of cases and controls (Table 2) (chi-square values being 0.004 and 0.233 respectively, $p>0.05$).

The association between p53 polymorphic genotypes and GCS on admission, GOSE, RHFUQ, QOLBRI-OS at 3 months and 6 months was statistically insignificant ($p>0.05$), chi-square values being 0.432,2.488,1.102,2.745, 0.002, 0.227, and 1.430 respectively. No statistically significant

gender difference was noted in the allelic distribution (chi-square 2.05).

Table 2: *Comparison of Arg72Pro polymorphism between cases and controls.*

Gene variant		Genotype frequency		χ^2 value
		Cases	Control	
CC	Observed	13	22	0.4741 (cases) (p=0.4741 q=0.525)
	Expected	13.03	21.12	
CG	Observed	29	26	
	Expected	28.92	27.75	0.2328 (Control) p=0.6034 q=0.393
GG	Observed	16	10	
	Expected	16.03	9.12	

There were no significant differences in GCS values between the three alleles of p53. However, the mean value of GCS was highest in patients with CC genotype (Table 3). Though there were no significant differences in the extended Glasgow outcome scale (GOSE) at 3 months and 6 months between the alleles, the highest score was observed in proline containing genotype (CC), suggesting a better outcome. The mean RHFUQ score was the lowest in patients with CC alleles, both at 3 months and 6 months suggesting a good recovery. The RHFUQ scores were on the higher side in patients with arginine containing genotypes of p53 (CG and GG) suggesting a bad prognosis (Table 3). The mean score for QOLIBRI-OS also showed the highest values among CC carriers at 3 and 6 months suggesting good recovery compared to CG and GG carriers (Table 3) Mortality among study subjects was noted only among GG and CG carriers. Whereas, among CC there were no deaths.

Table 3: *Comparison of Various Functional Outcome Scales in TBI patients with different genotypes of p53*

p53 genotype	CC	CG	GG	p-value
GCS N=58	12.08± 4.14 (n=13)	10.4±4.5 (n=19)	9±4.08 (n=16)	0.14
GOSE- 3 months N=44	6.4±1.9 (3,8) (n=12)	5.68±1.77 (2,8) (n=19)	4.38±2.5 (1,8) (n=13)	0.06
GOSE-6 months N=41	7±1.7 (n=12)	6.26±1.69 (3,8) (n=19)	6.6±1.26 (4,8) (n=10)	0.26
RHFUQ- 3 Months N=41	2.5 (0.25 7) (n=12)	5 (0 14) (n=19)	10.5 (3.5 22) (n=19)	0.3
RHFUQ-6 Months N=41	0 (0 3.2) (n=12)	1 (0 9) (n=19)	3 (1 7.25) (n=19)	0.3
QOLIBRI-OS-3 Months N=41	24.9±8.33 (7,30) (n=12)	24.6±6.03 (6,30) (n=19)	24.3±3.43 (19,30) (n=10)	0.25
QOLIBRI-OS-6 Months N=41	27.7±5.85 (11,30) (n=12)	25.4±6.8 (6,30) (n=19)	27.6±1.96 (25,30) (n=10)	0.16

Test: Kruskal wallis test; Values: Mean ±SD (min, max) (n) or Median (25% 75%)(n); p<0.05 significant*

Extended Glasgow Outcome Scores showed a significant improvement from 3 to 6 months among GG carriers (p=0.03). RHFUQ also showed a similar fashion of improvements with the p=0.05 among GG carriers. Whereas, QOLIBRI-OS showed significant improvement from 3 to 6 months among CC and GG carriers (p= 0.03 and 0.02 respectively) (Table 4). However, significant improvement was observed in all the TBI patients from 3 to 6 months irrespective of the gene variant. RHFUQ values were significantly lower compared to 3 months (p=0.03), GOSE values were significantly higher during 6 months follow up compared to 3 months (p=0.05). Similarly, QOLIBRI-OS values were significantly increased during 6 months (p=0.01).

Table 4: *Improvement recorded within the same genotype with every follow-up.*

		GOSE		RHFUQ		QOLIBRI-OS	
Genotype	Follow up	Score Mean ±SD(min, max) (n)	P value	Score Mean ±SD(min, max) (n)	P value	Score Mean ±SD(min, max) (n)	P value
CC	3 MONTH	6.42±1.98 (3,8) (n=12)	0.41	2.5 (0.25 7) (n=12)	0.116	24.9±8.33 (7,30) (n=12)	0.036*
	6 MONTH	7±1.71 (3,8) (n=12)		0 (0 3.2) (n=12)		27.7±5.85 (11,30) (n=12)	
CG	3 MONTH	5.68±1.77 (2,8) (n=19)	0.25	5 (0 14) (n=19)	0.322	24.6±6.03 (6,30) (n=19)	0.258
	6 MONTH	6.26±1.69 (3,8) (n=19)		1 (0 9) (n=19)		25.4±6.8 (6,30) (n=19)	
GG	3 MONTH	4.38±2.5 (1,8) (n=13)	0.03*	10.5 (3.5 22) (n=10)	0.05*	24.3±3.43 (19,30) (n=10)	0.020*
	6 MONTH	6.6±1.26 (4,8) (n=10)		3 (1 7.25) (n=10)		27.6±1.96 (25,30) (n=10)	

Test: Mann Whitney U test; Values: Mean ±SD (min, max) (n) or Median (25% 75%)(n); p<0.05 significant*

When taken account of 3 and 6 months of follow-up of all subjects without considering their genotype, it was noted that there were 3 deaths recorded making 6.82% of the population under study. Lower GOSE scores (2-5) were recorded in 34.09% and 21.95% during 3 and 6 months follow up respectively. A good prognosis (GOSE <5) was observed in 59.09% at 3 months and 78.08% at 6 months among the survivors (Table 5).

RHFUQ values were categorized as <10 and >10 ; <10 being considered good prognosis. About 70.7% showed a good prognosis at 3 months which increased to 80.49% at 6 months. Poor prognosis was noted in 29.26% of subjects in 3 months which was reduced to 19.51% during 6 months.

Table 5: Table showing follow up scores of patients for all questionnaires at 3 and 6 months

Questionnaire	Range	3 months N (%)	6 months N (%)
GOSE	1 (Dead)	3 (6.82)	0
	2-5	15 (34.09)	9 (21.95)
	>5	26 (59.09)	32 (78.04)
	Total	44	41
RHFUQ	<10	29 (70.73)	33 (80.49)
	>10	12 (29.26)	8 (19.51)
	Total	41	41
QOLIBRI-OS	<18	5 (12.2)	4 (9.76)
	<18	36 (87.8)	37 (90.24)
	Total	41	41

Health-related Quality of life was assessed using QOLIBRI-OS for all the subjects. The total score is divided as < 18 and >18, the latter being considered a good-quality index. Only 12.2% and 9.76% of subjects had scores below 18 at 3 and 6 months respectively. 87.8% of subjects scored good quality index at 3 and 6 months which increased up to 90.24% at 6 months (Table 5).

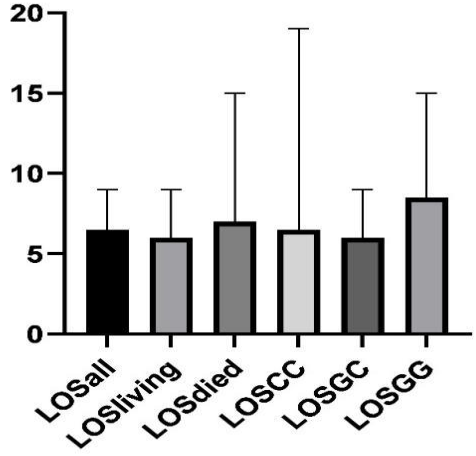

Figure 4: *Length of hospital stay among various subgroups of TBI patients (Median).*

The average length of stay in hospital (LOS) for all subjects was a median value of 6.5 (4 11.5) days (Figure4). Whereas for TBI survivors it was 6 (4 12.5) days and among diseased due to TBI average LOS was noted to be 7 (1, 10)days. As compared to CG 6 (4 9) and CC 6.5 (3.5 18.3) days, length of stay in the hospital was the highest for patients with GG 8.5 (5.5 13.5). The extent of improvement was shown by 1.09,1.10 and 1.27 in CC, CG, and GG respectively at 6 months as compared to 3 months by GOSE. Improvement by RHFUQ was 2.04, 1.48, and 2.39 respectively in the above-mentioned alleles. The degree of improvements in QOLIBRI was the same in all three gene variants. However, LOS was not statistically significant (p=0.689) in various genotypes.

The correlation of functional scores with the LOS in the hospital is as depicted in table 6.

Table 6: *Correlation of length of stay with various outcome scores*

		r	p
LOS & GOSE (n=41)	3 months	-0.3645	0.0191*
	6 months	-0.3050	0.05*
LOS & RHFUQ (n=41)	3 months	0.5368	0.0003*
	6 months	0.3366	0.0314*
LOS & QOLIBRI-OS (n=41)	3 months	-0.5253	0.0004*
	6 months	-0.2547	0.108

No correlation was observed between LOS and GOSE as well as LOS and QOLIBRI-OS scores. Whereas, a significant correlation was seen between LOS in days and RHFUQ scores at 3 and 6 months after injury.

The utility of the outcome assessment tools in assessing the recovery of patients after TBI was evaluated by ROC. The sensitivity, specificity, and AUC of RHFUQ were the highest (Figure 5 and 6) at 3 months as well as 6 months.

Among all the outcome tools used, RFHUQ3 was the most sensitive (85.7%) and specific (90%) with a cut-off value of 6.5. The area under the curve (AUC) was the highest for RFHUQ at 3 months (0.958) (Figure 5).AUC for QOLBRI was 0.114 at 3 months with a cut-off of 26.5, with low sensitivity and specificity of 19% and 15% respectively.

RFHUQ was the best outcome assessment tool at 6 months as well with the highest sensitivity of 100% and specificity of 91% and a cut-off value of 7.5. AUC was 0.968 (Figure 6).AUC for QOLBRI at 6 months was also low, 0.119,

with a cut-off of 24.5 with very low sensitivity and specificity of 25% and 10% respectively.

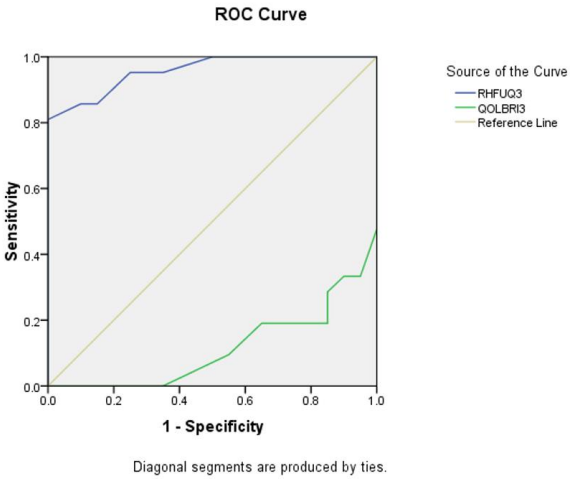

Figure 5: *ROC to Assess Functional outcome at 3 months*

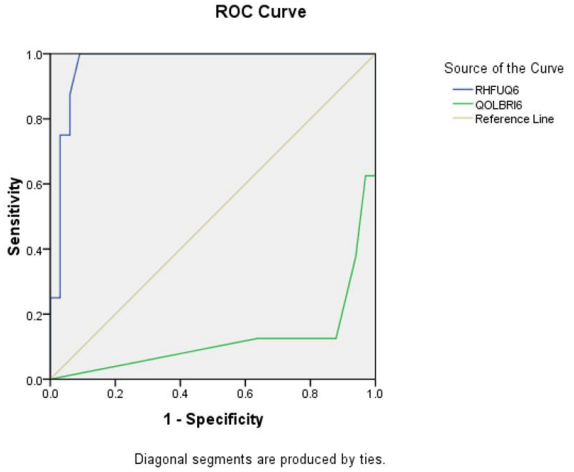

Figure 6: *ROC to assess outcome at 6 months*

IV. DISCUSSION

Homozygotic Arg72Arg, heterozygous Arg72Pro, and homozygous Pro72Pro are the different genotype expressions of p53. Based on the presence of arginine or proline, they can be homozygous dominant(GG), heterozygous(CG) and homozygous recessive(CC). G containing alleles code for arginine and C containing allelels code for proline.

In controls predominance of 'C' alleles was observed in the present study. Whereas in cases 'G' allele was predominant. However there was no significant difference. observed and expected allele frequencies as per HWE results ($p>0.05$).

Due to differences in electrophoretic mobility, several genotype variations were detected [8]. The p53 SNP has been linked to the outcome of TBI patients [29]. The two variants of the p53 protein, Arg/Arg and Arg/Pro, have distinct functional characteristics [9-12]. The Arg72Arg form induces apoptosis more effectively, whereas the Arg72Pro form stops the cell cycle at G1 and activates p53-dependent DNA repair [13-16]. The Pro72Pro allele of the Arg72Pro gene is found in 70 percent of South Africans and 23 percent of Western Europeans. According to the latitude gradient from Europe to Africa, the Pro72Pro allele appears to be a superior protection against sun-induced illnesses [17]. However, the few epidemiological studies that have looked at the Arg72Pro genotype and skin cancer risk differ [18,19].

Less mortality in Arg/Pro heterozygotes and Pro/Pro homozygotes compared to Arg/Arg homozygotes, which could be due to increased robustness caused by decreased proapoptotic activity and increased cell cycling arresting abilities of the Pro72 versus the Arg72 version of p53, thus protecting a person experiencing any critical illness [10,14,20].

GCS was to assess the severity of the injury and was highest in patients with CC (1.2-1.3 times) compared to other genotypes. This suggests insignificant association between the severity of the injury and the CC genotype of p53 (Table 3). GOSE scores were also the highest in CC genotype at 3 months and 6 months suggestive of a better recovery in proline-containing genotypes. Patients with CG and GG showed lower moderate disability at 3 months and upper-moderate disability at 6 months, whereas CC genotype showed upper moderate disability at 3 months and lower good recovery at 6 months.

RHFUQ questionnaire that compares patients' experience before and after injury also showed a similar tendency in the recovery pattern. A higher score suggests a bad recovery and vice versa. The highest score was observed in patients with GG (though insignificant) implying a poorer recovery in those patients. Minimum scores were noted in CC genotypes at 3 months and 6 months (table 3).RHFUQ was

designed to evaluate functional and social outcomes (at the level of disability), a short and simple measure that would be straightforward to use and to analyze was needed. RHFUQ questionnaire is a good clinical tool that gives an overall estimate of experiences and problems of patients on daily basis after head injuries. It covers disability and consequences of loss of function or impairment. RHFUQ questionnaire was found to be very effective and comparable to GOSE, with the highest area under the curve at 3 months as well as at 6 months when ROC was drawn (Figure 5 and Figure 6). The questionnaire also showed the highest sensitivity as well as specificity.

It is the fact that the disability is influenced by the associated injuries, response to the injury, previous injuries sustained, and personal and social circumstances of patients. The rating scale rather than simple "yes/no" responses extends its range to reflect the disparity in the outcomes of injury for patients, the circumstances of whose injuries vary enormously. This questionnaire has been at par with the performance GOSE in assessing day-to-day activities.

Quality of life after brain injury- overall score (QULBRI) assesses overall wellbeing of the patients, with the maximum score being 30 suggesting a good/ satisfied life and lowest being 6 with least satisfaction. QOLIBRI-OS scores are the highest for CC genotypes at 3 as well as 6 months (table 4). However, QOLBRI at 3 and 6 months showed a low area under the curve on constructing ROC (Figure 5 and 6), also the lowest sensitivity as well as specificity as compared to other questionnaires. Even though the outcome scores were the least in GG genotypes, the extent of recovery was the highest in them. This finding is justified by their longest length of stay (Figure 4).

Significant Positive correlation of RHFUQ scores at 3 and 6 months and LOS suggests a longer length of hospital stay among people with poor outcomes (Table 6). This correlation is on par with the patient's condition and psychosocial factors. We can say that, in addition to gross recovery from the traumatic condition as well as recovery in terms of health-related queries, longer hospital stay which was noted among those who scored more in RHFUQ suggests that patients psychosocial recovery is also an important factor in overall recovery and patient rehabilitation in this regard has to be improved. This finding is also supported by the ROC (Figure 5 and 6).

TBI recovery is variable and relies on the patient's age as well as the nature, location, and extent of the injury [21,22]. Only a small portion of the variation in outcomes is explained by known predictors. Martinez PL et al. published a prospective research in 2005 that included 90 Caucasian patients with severe TBI and 100 healthy controls[7]. In comparison to controls, the study found no significant changes in the frequency of Arg72Pro polymorphisms. The Glasgow outcome scale was used to assess TBI outcomes at discharge and six months. According to the findings, the Arg/Arg genotype was linked to 69 percent of negative outcomes. It was also discovered that Arg/Arg variations had a 2.9 times higher probability of having a poor discharge result. The length of stay in the hospital did not differ significantly between individuals with the Arg/Arg genotype and those with the Arg/Pro and Pro/Pro genotypes. The analysis found no link between mortality and the Arg/Arg polymorphism [7]. At six months after TBI, there was a statistically significant difference in genotypes and a poor prognosis.

Another study by Martinez PL et al., recruited 90 patients with severe TBI patients and Glasgow outcome scale at discharge being the outcome assessment tool, reported that 81.1% of patients had a poor outcome and 18.9% of them had a good outcome. The results clearly indicated that Arg/Arg polymorphism was an independent predictor of poor outcome, the risk of a poor outcome being 3.55 times greater with Arg/Arg genotypes which was in agreement with their previous report [23].

Mohammed Ali HA et al found similar results in their study, which enrolled 51 Sudanese TBI patients, of whom 84.31 percent were discharged with a favourable outcome. Arg/Arg

genotypes were found in 69.76 percent of patients who had a favourable result, 11.62 percent in Arg/Pro genotypes, and 6.98 percent in Pro/Pro genotypes. Approximately 13.72 percent of patients had a terrible outcome, with 71.42 percent dying and 28.57 percent having a poor prognosis. One patient was most likely unable to be followed up on. The study found that patients with the Arg/Pro and Pro/Pro alleles had a 100% survival rate [24].

Eighty percent of the deaths showed Arg/Arg alleles suggesting a poor prognosis in arginine containing variants.

V. CONCLUSION

It could be concluded from the study that no significant association between p53 gene polymorphism and functional outcome after TBI was observed. However, patients with CC genotype (proline/proline) had less severe injuries, whereas the extent of recovery was maximum in GG-containing genotypes, supported by their longest length of hospital stay. RHFUQ was the most sensitive and specific tool to assess the functional outcome after TBI when GOSE is the gold standard.

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ABBREVIATIONS

GCS = Glasgow Coma Scale; GOSE = Extended Glasgow Outcome Scale; RHFUQ= Rivermead Head Injury Follow-up Questionnaire; QOLIBRI-OS= Quality of Life after Brain Injury- Overall Scale

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