EVALUATION OF ANTICOAGULATION IN POST-SURGICAL PATIENTS WITH MECHANICAL VALVE REPLACEMENT

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ABSTRACT:

INTRODUCTION: Mitral, aortic, tricuspid, and pulmonary valve disease are the four types of valvular heart disease. Valvular heart disease is defined by damage to or a congenital abnormality in one or more of the heart's valves. Rheumatic heart disease is the term used to describe valvular heart disease that develops as a consequence of rheumatic fever. There have been several suggestions made regarding biomarkers that might be used for tracking the aetiology of aortic valve disease; however, not all biomarkers are candidates that are clinically helpful. Patients who are taking vitamin K antagonists are typically advised to have their blood tested using the international normalised ratio. The purpose of this study was to determine the mean international normalised ratio in patients diagnosed with valvular heart disease who had had mechanical valve replacement and were on anti-coagulant medication.

AIMS & OBJECTIVE: The purpose of this study was to determine the mean international normalised ratio in patients diagnosed with valvular heart disease who had had mechanical valve replacement and were on anti-coagulant medication.

MATERIAL & METHODS: Between the dates of 28 July 2020 and 28 January 2021, the research was carried out at the Department of Cardiology at the Punjab Institute of Cardiology in Lahore. After the inclusion criteria were satisfied, a total of 250 patients were enrolled. Consent after being fully informed was obtained, as well as demographic information. Then patients underwent surgery. After 3rd month patients who were on standard anti-coagulation therapy as per hospital protocol were assessed. On each visit, blood sample was taken by using 3cc disposable syringe and sent to the laboratory of the hospital for assessment of INR and serial values of INR.

RESULTS: The mean age of the patients was 42.51±16.59 years, there were 149(59.60%) patients were male. Hypertension and diabetes mellitus was found in 103(41.2%) & 75(30%) patients respectively. After 3rd month the mean INR value of patients was 2.245±0.4016.

CONCLUSION: The mjority of patients had subtherapeutic INR at baseline but during follow up at INR clinic the patients showed marked improvement in their INR levels. So all patients who had valve replacement must be followed up in a specialized clicinic so that we can have better management of these patients.

KEY WORDS: Valvular Heart Disease, International Normalized Ratio, Mechanical Valve Replacement.

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INTRODUCTION:

It wasn't until the 1960s that the concept of replacing human valves with mechanical ones was first brought up. On March 11, 1960, a flexible polyurethane valve was used to perform the first ever prosthetic valve replacement in a human patient. The patient was a 44-year-old female.[1-2] After having a bioprosthesis placed in the aortic valve, the recommendations of the American College of Cardiology recommend taking anticoagulant medication for a period of three months. However, there is still a tremendous deal of diversity in the clinical practise that is currently being used, and the outcomes of clinical investigations are often contradictory.[3] Anti-thrombotic therapy following valve replacement can refer to a variety of various scenarios depending on the specifics of the patient's condition. Vitamin K antagonists are used for the long-term anticoagulation of mechanical prostheses, and the target international normalised ratio is customised to the individual patient's needs as well as the features of the prosthesis.[4]

The American recommendations make a systematic mention of the relationship between low-dose aspirin and heart disease, but the European guidelines are more restrictive. Early heparin treatment is routinely utilised early on following mechanical valve replacement, despite the fact that there are no specific recommendations regarding the timing, kind, or amount of the medicine to be administered.[5] At this time, individuals who have mechanical prostheses should not take anticoagulants that may be taken directly by mouth. The fact that bioprostheses do not require continuous anticoagulant treatment is the primary benefit of these devices.[6] The addition of aspirin to oral anticoagulants after MVR provided the benefits of being safe, convenient, and dependable. There was no need to constantly change the dosages of the oral anticoagulants, and there was no risk of thromboembolic events.[2]

One study reported that the mean INR was 2.1 ± 0.8 in patients after valvular heart replacement therapy.[7] In another trial, the mean INR was 1.91 ± 0.23 in the low-INR (low-dose aspirin) group, and 2.59 ± 0.26 in the conventional-INR (high dose aspirin) group (P < 0.001).[8] Rationale of this study is to assess the mean international normalized ratio after mechanical valve replacement in patients with valvular heart disease. Literature showed that there is high INR level with anti-coagulation use after valvular heart replacement therapy. But in routine, patients are prescribed anti-coagulants to normalize the blood

flow and clotting profile which may alter the INR level and cause bleeding in earlier or later stages.

But not much work has been done in this regard. And also there is lack of local literature. So we want to conduct this study to get local evidence which could help us in determining the extent of problem in local population and we can implement the results in local setting and alter some treatment protocol of the patients who underwent mechanical valve replacement in order to improve the outcome and also can recommend to screen the factors affecting INR after surgery. This will help us to plan strategy to alter some treatment protocol to prevent the complications of adverse outcome of mechanical valve replacement.

METHODOLOGY:

Between the dates of 28 July 2020 and 28 January 2021, the research was carried out at the Department of Cardiology at the Punjab Institute of Cardiology in Lahore. Each patient provided their permission after receiving appropriate information. Their demographic information (name, age, gender, type of valvular heart disease, h/o diabetes (BSR>186mg/dl), hypertension (BP≥140/90mmHg) or smoking (>5 pack year), taking anti-coagulants) was also noted. The inclusion criteria were patients of age 16-70 years presenting with valvular heart disease. Patients with renal dysfunction (creatinine>1.2mg/dl), liver dysfunction (AST>40IU, ALT>40IU, bilirubin >5mIU) and thalassemia or bleeding profile (PT>20sec, INR>2) before diagnosis of valvular heart disease (on medical record).

Sample size of 250 patients was calculated with 95% confidence level, d=1% and taking magnitude of mean INR i.e. 2.1 ± 0.8 in patients after valvular heart replacement.[7] Patients underwent surgery by a single surgical team to control bias in the study. Then all patients were followed-up in INR clinic for 3 months after surgery. After 3rd month patients were given standard anti-coagulation therapy as per hospital protocol. On each visit, blood sample was taken by using 3cc disposable syringe and sent to the laboratory of the hospital for assessment of INR and serial values of INR. The term "valvular heart disease" (VHD) refers to a condition diagnosed by echocardiogram that has persisted for more than six months and affects one or more of the four cardiac valves (the aortic and bicuspid valves on the left side, and the pulmonary and tricuspid valves on the right side). Mean INR was measured after 3 months of surgery. It was assessed on various blood.

INR = [PT patient/Normal patient] 1st. 1st value depends on KIT

The collected data was analysed statistically by using SPSS version 25. Quantitative variables like age and serial INR was presented in form of mean and standard deviation. Qualitative variables like gender, type of valvular heart disease, h/o diabetes (BSR>186mg/dl), hypertension (BP≥140/90mmHg) or smoking (>5 pack year) was presented in form of frequency and percentage. P-value≤0.05 was taken as significant.

RESULTS:

In this study the mean age of the patients was 42.51±16.59 years with minimum and maximum ages of 16 and 70 years respectively. Among 250 patients, there were 149(59.60%) patients were male and 101(40.40%) patients were females. Male to female ratio of the patients was 1.47:1. (Figure-1) The study results showed that among 250 patients the hypertension was found in 103(41.2%) patients. Of 250 patients the history of diabetes mellitus was noted in 75(30%) patients. In this study the smoking status was found in 74(29.6%) patients.

Out of 250 patients, 86(34.40%) patients had single valvular heart disease, 85(34%) patients had double and 79(31.60%) patients had triple valvular heart disease.(Figure-2) In this study at baseline the mean INR value of patients was 1.345±0.402 with minimum and maximum values

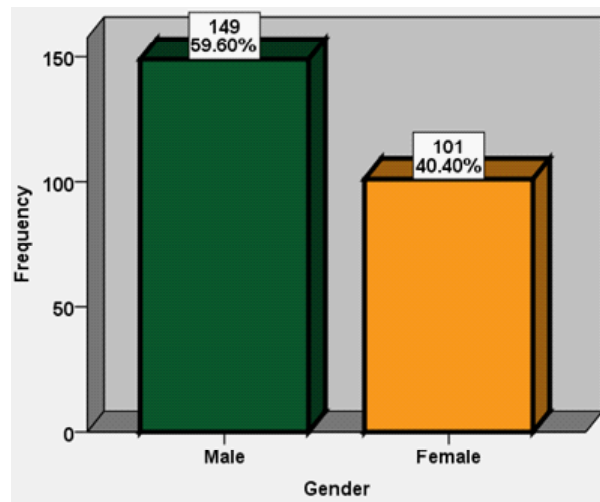**Figure 1: Frequency distribution of gender**

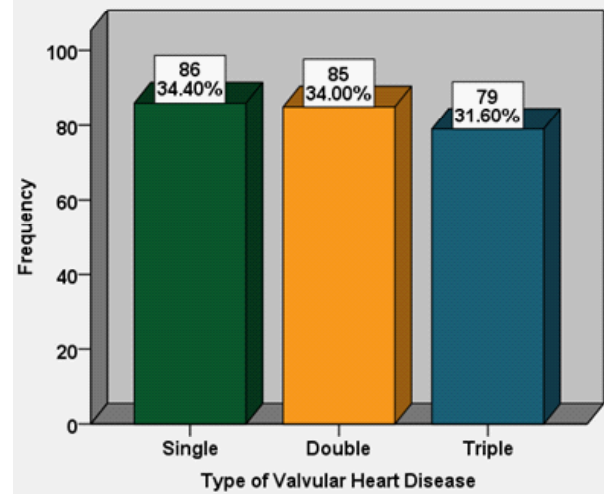**Figure 2: Frequency distribution of type of valvular heart disease**

Table-1: INR levels at baseline.	
Therapeutic range	Total Patients (250)
Less than 2	233
2 - 5	17
>5	0
Mean	1.345 ± 0.402

Table-2: INR levels at 3 months.	
Therapeutic range	Total Patients (250)
Less than 2	72
2 - 5	178
>5	0
Mean	2.245 ± 0.4016

of 0.7 & 2.0 respectively. 233 patients had INR <2 and seventen patietns had INR between 2 to 5. No patients had INR > 5. (Table-1) In this study after 3rd month the mean INR value of patients was 2.245±0.4016 with minimum and maximum values of 1.5 & 2.9 respectively. 72 patients had INR <2 and 178 patietns had INR between 2 to 5. No patients had INR > 5. (Table-2)

DISCUSSION:

This present descriptive case series study was carried out at the Department of Cardiology, Punjab Institute of Cardiology, in Lahore, Pakistan,

with the goal of determining the mean international normalised ratio with anti-coagulation use in patients with valvular heart disease who had undergone mechanical valve replacement. Patients who take an active role in the management of their health have better clinical outcomes related with chronic oral anticoagulation. The strength of the anticoagulant medication and the length of time the international normalised ratio (INR) is higher than the therapeutic goal range are directly linked to the risk of bleeding following heart valve replacement. The number of INR measures taken by patients is increased when they are permitted to perform their own testing, which results in an increase in the amount of time that their INR is within the therapeutic range.[9-10]

In comparison to the Caucasian population, the Asian population was shown to have a higher incidence of intracerebral haemorrhage as a subtype of stroke. There is not one single theory that may adequately explain the higher incidence of intracranial haemorrhage in Asian populations.[11] A lower INR level was typically recognised as being suitable for anticoagulant medication in the limited trials that were completed in Asian populations who had mechanical heart valve replacement.[12]

In this particular study, the mean INR value of patients at the beginning of the trial was 1.345 0.402, and the mean INR value of patients after the third month was 2.245 0.4016. It has been debated in Japan what the ideal PT-INR should be, and the majority of those papers issued a caution that the worldwide standard value of 2.5-3.5 that has been established as the clinical therapeutic range in Europe and the United States is too high for Japanese patients. There have been many different findings, some of which suggest that the appropriate clinical range should be established at 1.6-2.8, and that 2.0-3.0 is desirable for the instances with high risk for thromboembolism.[13-15]

One study reported that the mean INR was 2.1±0.8 in patients after valvular heart replacement therapy.[7] In a different study, the traditional INR (high dosage aspirin) group had a mean INR of 2.590.26, whereas the low-dose aspirin group had a mean INR of 1.910.23 (P 0.001).[8] In a prospective randomised multicenter trial, Heinrich Koertke et al., 201016 followed 1137 German patients and demonstrated the efficacy and safety of very low, self-managed INR doses in patients with aortic valve replacement (INR target value: 2.0, range: 1.6–2.1), as well as in patients with mitral valve or double valve replacement. The INR target value was 2.0, and the range was 1.6–2.1. (INR target value: 2.3, range: 2.0–2.5).

Misawa and his coworkers reported on their clinical experience with 44 aortic valve replacements using a Bicarbon prosthesis. These patients were treated with reduced intensity anticoagulation (therapeutic INR range of 1.3–1.8) coupled with anti-platelet agents. Misawa and his coworkers also discussed their findings (either dipyridamole or aspirin). These authors had a dishearteningly high rate of thromboembolism, reaching as high as 1.16% per patient per year; as a result, they decided to stop this decreased intensity programme.[17] According to the findings of the AREVA study conducted in France, the incidence of thromboembolic complications was comparable between patients with a target INR range of 2.0–3.0 and patients with a target INR range of 3.0–4.5. On the other hand, the low-dose group experienced a lower incidence of bleeding complications.[18] Analyses of the prothrombin time (PT) and international normalised ratio (INR) were carried out on 213 patients using warfarin. The results showed that the PT (19.43.1 seconds) and the INR (1.90.6) in the normal group were essentially compatible with those reported in domestic research.[19-20]

In recent years, there has been a progressive promotion of an expanding number of anti-coagulant medications, each of which has a quick start and a long-lasting impact compared to that of warfarin. However, the amount of time it takes for such treatments to be brought to market is quite short, the price of such drugs is rather high in comparison to the cost of warfarin, and there have not been any large-scale controlled trials done to test the drugs' effectiveness and safety as of yet. As a result, there is a need for more research to prove the usefulness and safety of these pharmaceuticals. [21-23] Itthidet Kamthornthanakarn and Rungroj Krittayaphong[24] conducted a study that indicated in their study that the ideal INR level was within the range of 2.0 to 3.4 in our cohort of Thai patients who had undergone mechanical mitral valve replacement. The proportion of time spent by patients within the INR 2.5–3.4 range, within the INR 2.5 range, and within the INR > 3.4 range was, respectively, 41.96, 54.04, and 4%. The total event rate was at its lowest when the INR was in the range of 2.0 to 3.4.

CONCLUSION:

The majority of patients had subtherapeutic INR

at baseline but during follow up at INR clinic the patients showed marked improvement in their INR levels. So all patients who had valve replacement must be followed up in a specialized clinic so that we can have better management of these patients.

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