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Original Articles

Intention to Consume Alcohol among Dayak Adolescents in Sarawak: An Application of Theory of Planned Behavior

Comparative Evaluation of Effectiveness of Rocuronium Bromide vs. Succinyl Choline on Quality of Intubating Conditions during General Anesthesia

Thyroid Profile and Serum Lipid Level in Women with Normal Pregnancy

Outcome of Posterior Cruciate Ligament Avulsion Fractures from Tibial Attachment Treated by Open Reduction and Internal Fixation

Conservative Management of Pott's Spine and Its Outcome: An Institute-Based Observational Study

Association between Comorbidities and COVID-19 Mortality: A Cross-Sectional Study in a Community Health Center in Indonesia

Comparison of Coagulation Parameters between Severe and Non-severe COVID-19 Patients Treated in a Tertiary Hospital in Indonesia

Correlation between Acute Phase Symptoms with Neurological Long Covid Symptoms on COVID-19 Survivors

Case Reports

Crowned Dens Syndrome: A Rare Cause of Sudden Onset Neck Pain

Paradoxical Hemiparesis from Cerebellopontine Angle Tumor: A Case Report

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Original Article

Intention to Consume Alcohol among Dayak Adolescents in Sarawak: An Application of Theory of Planned Behavior

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Abstract

Objectives: To explore the application of a model that integrates various factors that influence Dayak adolescents' intentions to consume alcohol in Sarawak, Malaysia.

Methods: A cross-sectional quantitative study was conducted from September 2019 to February 2022. Through multistage stratified cluster sampling, 12 districts were selected from 12 divisions. Respondents were selected randomly and were interviewed using a questionnaire.

Results: Structural equation modeling was used to test the Theory of Planned Behavior (TPB) and explore the relationship between various variables and respondents' intention to consume alcohol. The findings suggest that attitude (β =.22, p<.001), subjective norm (β= 33, p<.001), and perceived behavior control (β=−.41, p< .001) influenced the intention to consume alcohol. In contrast, alcohol consumption was associated with intention (β=.15, p < .001), attitude (β= .20, p< .001), and perceived behavior control (β=−.32, p< .001).

Conclusion: The findings demonstrated that the TPB model can be used to explore various variables that influence the intention to consume alcohol among Dayak adolescents, with attitude, subjective norm, and perceived behavior control as the variable influencing the intention. This highlights the need for paying attention to those variables when developing age-appropriate strategies that address various social levels to curb alcohol consumption. Given the concerning rates of risky drinking and dependency, school-based health initiatives and focused screening for Dayak adolescents are crucial.

Keywords: Adolescents, alcohol, dayak, theory of planned behavior

Introduction

The psychoactive component of alcohol is ethanol, a molecule containing carbon atoms and the hydroxyl (-OH) group. It is commonly referred to as ethanol or ethyl alcohol and is known to have stimulant effects. Ethanol is produced through fermentation and distillation and is a key ingredient in various beverages, including wine, beer, and hard liquor.[1] Early alcohol use was believed to be detrimental to the adolescent brain's development, particularly in those who began drinking before or by age 15.[2] Such individuals may experience alcohol-related problems later in life, including dependency and a consistent pattern of high alcohol use.[3] These problems can lead to physical or mental disorders, as described in the Diagnostic and Statistical Manual of Mental Disorders.[4] Alcohol use disorder, previously known as alcoholism or alcohol dependence, is characterized by excessive alcohol consumption that causes personal or professional problems, an inability to regulate drinking, and the need for increasing amounts of alcohol to achieve the same effects.[5] Alcohol consumption in Malaysia has steadily risen, increasing from 0.8 liters in 2005 to 1.7 liters in 2015 per person.[6] However, the prevalence of alcohol usage in

Malaysia is lower than in other Western Pacific nations, with only 8.0% of Malaysian adults regularly consuming alcohol. The proportion of older persons who drink has declined from 7.8% in 2006 to 4.0% in 2015.[7] It is worth noting that the "Bumiputras" population in Malaysia has the highest percentage of alcohol consumption, with 21.6% of them consuming alcohol in 2015. Furthermore, 75% of "Bumiputras" engaged in binge drinking. Although the prevalence of binge drinking has decreased since the previous survey in 2011, there has been an increase among current drinkers and adolescents.[6] Sarawak is one of the states in Malaysia with the highest percentage of current drinkers, with more than one-fifth of the population, or 500,000 individuals, currently consuming alcohol. Interestingly, urban areas had a larger proportion of current drinkers than rural areas, men, and those with higher levels of education.[8] Predicting alcohol consumption, the Theory of Planned Behavior (TPB) is a popular model, particularly for adolescents.[9,10] This model assumes behavioral intentions are the precursors to behavior rather than attitudes. Attitude, subjective norms, and perceived behavioral control influence the intention. Each of these factors has its own set of influencing factors. The attitude variable represents the perceived likely qualities of the behavior. In contrast, the subjective norm represents perceptions of others' specific preferences on whether or not one should engage in the conduct. Perceived behavioral control is similar to the idea of self-efficacy and is the belief that a person's behavior is under their control. Implicit attitudes toward alcohol, in addition to readiness and intention to drink, which develop over time with regular exposure to alcohol, may influence risky drinking in young individuals, according to Davies *et al*.[11] Binge drinking was more likely to be reported by those with a positive attitude toward it and considered it socially acceptable and manageable behavior.[10] Anti-alcohol and pro-abstinence social systems comprising friends, family, and community were linked to greater anti-alcohol subjective norms and attitudes among teenagers, according to Zhao *et al*.[12] Adolescent alcohol consumption is rising worldwide,[13] particularly in Malaysia.[14] Even though adolescents rarely drink, they consume more alcohol on each occasion than adults.[15] Identifying the high-risk group is critical to developing a more effective and viable intervention, as these people are more likely to become high-risk alcohol drinkers.[16]

This study examined a model incorporating several factors on the intention to consume alcohol among Dayak adolescents in Sarawak, Malaysia.

Methods

This cross-sectional study aimed to explore alcohol consumption among Dayak adolescents in Sarawak. The emphasis on the Dayak communities stems from their distinct cultural distinctions. While numerous native groups reside in Sarawak, each with its language, traditions, and cultural practices, they share certain recognizable characteristics. The sample population size was estimated using the precision-based approach single proportion formula, which accounted for a 19% base population proportion of current drinkers in Sarawak[17] and a 5% absolute precision. Respondents were randomly chosen from male and female respondent houses, with only male or female adolescents approached accordingly. The sample size was inflated to reach 1510 Dayak adolescents, and multistage stratified cluster sampling was used to choose 12 districts from each of the 12 divisions. Face-to-face interviews using an interviewer-administered questionnaire were conducted in Malay, and the questionnaire was pilot-tested to ensure its quality before data collection. Ethics approval from the ethics committee of the Faculty of Medicine and Health Sciences was obtained before data collection. (Ref: UNIMAS/NC-21.02/03-02 JId.4 (55), 20 April 2020).

The study was conducted over 30 months, from September 2019 to February 2022, with a breakdown of different activities, including proposal approval, pretesting and validation and data collection and analysis. The questionnaire consisted of five components: respondent characteristics (age, education, occupation, marital status, education status, ethnicity, and religion), parental characteristics (age, gender, monthly household income, spouse and child relationships, and family characteristics), the Theory of Planned Behavior, alcohol consumption characteristics (frequency of drinking and alcohol misuse), and the type of alcoholic beverages consumed (assessed using the AUDIT questionnaire). The Theory of Planned Behavior measured attitude, social norms, perceived behavior control, and intention to consume alcohol among Dayak adolescents. Ten questions were asked to identify the alcohol use disorder among the Dayak adolescents, commonly known as AUDIT: The Alcohol Use Disorders

Mohd Faiz Gahamat, Md Mizanur Rahman, *et al*

Identification Test.[18] The AUDIT was developed as a simple method of screening for excessive drinking and to assist in brief assessment. It has three domains of assessing the hazardous alcohol use, dependence symptoms and harmful alcohol use. The Theory of Planned Behavior (TPB), 68 statement has been used to predict risky drinking. It measured attitudes, subjective norms, and perceived behavioral control that predict intention to engage in risky drinking, which in turn predicts future heavy episodic drinking.[19] Back-to-back translation was validated by two language experts, who are expert in both Malay and English languages. All the questionnaire were pre-tested in local setting consistency. The Cronbach's alpha reliability coefficient varies from .876 to .946. A measurement model was developed to determine the convergent and discriminant validity of the constructs.[20] Informed written consent was obtained from guardians and adolescents before data collection. Structural equation modeling (SEM) was used to establish the causal relationship between attitude, subjective norm, perceived behavior control, intention to use, and alcohol intake among Dayak adolescents. SEM analysis used a measurement model (convergent and discriminant validity) and structural model analysis (path analysis). The variance accounted for (VAF) was used to analyze different parameters' indirect and total effects on the variables.[21] Partial least squares were used to analyze the relationship between constructs, with p-values of regression coefficients (F-test) and variance explained (R-squared) as indicators of the model's explanatory power.[22] Bootstrapping was used to assess the statistical significance of each path.[21]

Results

The Table 1 illustrates the socio-demographic characteristics of the participants. The survey of 1,510 respondents found that the average age was 17.3 years, with a slight majority of females (56.6%). The Iban community was the most represented ethnic group (68%), followed by the Bidayuh (14.6%) and the Orang Ulu (5.9%). Christianity was the most widely held religion (91.7%), followed by Islam (5.8%) and Buddhism (2.1%). Most respondents were single (91%), with students making up the majority of the workforce (77.7%). Secondary schooling was the most common level of education (64.5%), followed by pre-university (25.6%; Table 1).

The results show that 50.0% of Dayak adolescents used alcohol at a low risk, while 31.0% consumed alcohol at a hazardous

Table 1 Respondents Characteristics (n=1510)

Characteristics	N	%/Mean
Age in years, min, max	1510	17.30 (1.44), 11, 19
Gender		
Male	656	43.4
Female	854	56.6
Ethnicity		
Iban	1026	67.9
Bidayuh	220	14.6
Orang Ulu	89	5.9
§Others	175	11.6
Religion		
Christian	1385	91.7
Islam	87	5.8
Buddhist	31	2.1
¥Others	7	0.5
Marital status		
Single	1374	91.0
Married	91	6.0
€Others	45	3.0
Occupation		
Student	1174	77.7
Unemployed	42	2.8
Housewife	5	0.3
ξOthers	289	19.1
Education level		
No formal education	10	0.7
Kindergarten	3	0.2
Primary school	47	3.1
Secondary school	974	64.5
Pre-university	386	25.6
Vocational school	6	0.4
ΨOthers	84	5.6

§others include Kayan, Punan, Ngaju, etc; ¥others include Bahai, Animism, etc; €others include separated, divorced etc; ξothers includes employed, self-employed, etc; Ψothers include Diploma, Certificate, etc

Table 2 Alcohol use disorder (n=1510)

Alcohol use disorder	n	%
No risk (0)	174	11
Low-risk (1–7)	752	50
Hazardous (8–15)	465	31
Harmful (16-19)	70	5
Dependence (≥20)	49	3

ξ others include whiskey, sake, tequila, etc.

risk. Abstainers comprised only 11.0% of the participants, while a small number (5.0%) exhibited harmful or dependent alcohol use, with 3.0% falling under this category (Table 2).

A non-linear algorithm and bootstrapping resampling method were used to conduct a robust path analysis. Five constructs were evaluated to test for validity, including physical activity, dietary behavior, perceived behavior control, subjective norm, attitude, intention, and alcohol consumption. The average variance extracted was used to assess convergent validity, with a value greater than 0.50 indicating that the latent construct accounts for most of the variation in the indicators. The AVE extracted ranged from .58 to 1.00, indicating good reliability. Discriminant validity was assessed using three measures: the Fornell-Larcker criteria, item

cross-loading, and the Heterotrait-Monotrait (HTMT) criterion ratio. The standardized root mean squared residual (SRMR) was .09, which is acceptable, and the normed fit index (NFI) was .58, indicating a well-fitted model.

Fig. 1 presents the results of the analysis and the hypothesis decision. Attitude, subjective norm, and perceived behavior control were associated with intention. Attitude (β= .22, $p<.001$) and subjective norm (β=.33, $p<.001$) were positively associated with intention, while perceived behavior control (β=−.41, $p< .001$) was negatively associated with intention. Intention, attitude, and perceived behavior control were also associated with alcohol consumption among Dayak adolescents. Intention (β=.15, $p<.001$) and attitude (β =.20, $p<.001$) had a direct positive effect on alcohol consumption, while perceived behavior control (β=−.32, $p<.001$) had a strong negative effect on alcohol consumption. However, no significant association was found between subjective norms and alcohol consumption. Therefore, subjective norms had no association with alcohol consumption among Dayak adolescents (Fig. 1).

Discussion

The analysis revealed that alcohol consumption and problematic drinking were more likely to be engaged in by older Dayak adolescents,
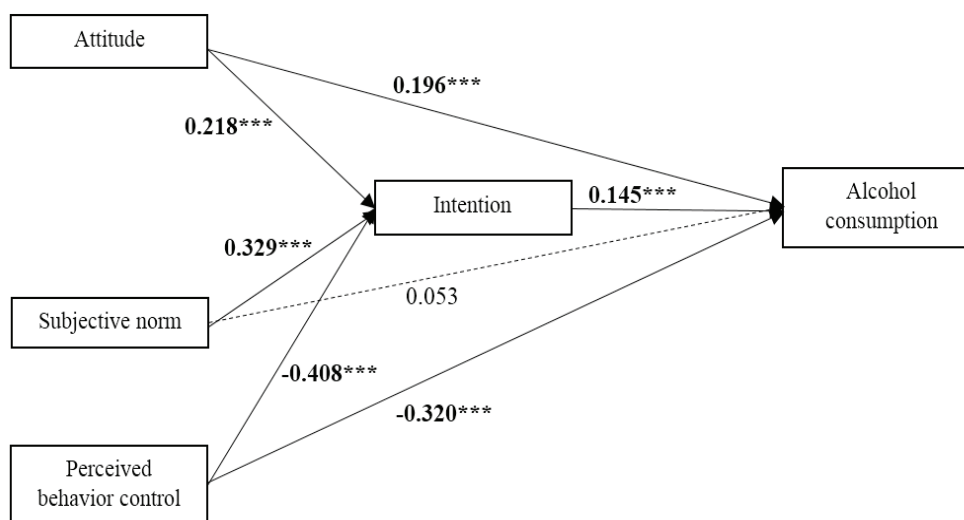
Fig. 1 Structural Path Analysis of the Alcohol Consumption, Intention, Attitude, Subjective Norm, and Perceived Behavior Control

Mohd Faiz Gahamat, Md Mizanur Rahman, *et al*

consistent with a study conducted in Australia.[12] This might be due to the greater availability of alcohol in Sarawak, particularly during social events and festivals, compared to other areas in Malaysia. However, the study also suggests that the role of direct or indirect availability, such as through parents or family members, should be further investigated.[23] The findings of this study indicated that stronger intentions to drink and higher alcohol consumption were associated with a higher attitude score among Dayak adolescents, contradicting the findings of another study by Sudhinaraset *et al.*[24] The latter found that lower involvement in social networks that use alcohol, less peer persuasion to use, and stronger negotiation skills to resist alcohol use was linked to parental or societal disapproval or negative attitudes towards alcohol use. In this study, subjective norms were associated with drinking, which aligns with the findings of Pedersen,[25] who found that specific drinking outcomes were linked with perceived descriptive norms or the peer's perception of alcohol use. However, further research is needed to assess the perceived injunctive norms, or individuals' perceptions of peers' attitudes towards the acceptability of certain behaviors, associated with all drinking outcomes, including consequences. The perceived behavior control had a negative association with intention and alcohol consumption. While exposure to information about the harmful effects of alcohol is crucial for preventing alcohol consumption, other control factors, such as the legal and economic ways of obtaining alcohol among adolescents, were significantly more beneficial.[11] This TPB model suggests that intention is the strongest predictor of alcohol use. This means that the more someone intends to drink alcohol, the more likely they are to actually do so. Intention is influenced by a number of factors, including attitudes, subjective norms, and perceived behavioral control.[26] However, it is important to note that the relationship between intention and behavior could be a complex and might be influenced by other factors such as past drinking behavior and the social environment. Overall, in this study highlights the complex interplay between intentions, social environment, and contextual factors in predicting drinking alcohol among Dayak adolescents. Several limitations should be considered when interpreting the findings of this study. Firstly, caution should be exercised when generalizing the results to other ethnic groups or regions since the study focused exclusively on the Dayak adolescents of Sarawak. Additionally, relying on self-reported data, which may be susceptible to biases in perception, may have influenced the accuracy of the findings.

Furthermore, the study's cross-sectional design limits its ability to establish a causal relationship between the independent and dependent variables. Therefore, the conclusions drawn from this study should be interpreted with caution, and future research should address these limitations to provide more robust and reliable evidence.

In conclusion, this study sheds light on the alcohol consumption patterns and associated factors among Dayak adolescents in Sarawak. The findings suggest that a significant proportion of Dayak adolescents are engaging in alcohol consumption at either low or hazardous levels, with a small percentage exhibiting harmful or dependent alcohol use. Attitude, subjective norm, and perceived behavior control were associated with intention, while intention, attitude, and perceived behavior control were associated with alcohol consumption among Dayak adolescents. However, subjective norms did not have a significant association with alcohol consumption. These findings highlight the importance of developing interventions such as school-based health promotion, and targeted screening among adolescent population that focus on changing attitudes, strengthening perceived behavior control, and improving parental and societal disapproval of alcohol consumption. Future research should consider addressing the limitations of this study and exploring the underlying factors that contribute to alcohol consumption among Dayak adolescents in Sarawak.

Acknowledgements

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Comparative Evaluation of Effectiveness of Rocuronium Bromide vs. Succinyl Choline on Quality of Intubating Conditions during General Anesthesia

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Abstract

Objectives: To compare the quality of intubating conditions and hemodynamic responses to the administration of Rocuronium Bromide and Succinyl Choline during general anesthesia.

Methods: This was a comparative study conducted at the anesthesiology department of a tertiary care medical college. Sixty patients undergoing various surgeries under general anesthesia were included in this study based on predefined inclusion and exclusion criteria. Patients were divided into Group S (receiving succinylcholine) and Group R (receiving rocuronium). In all patients, the quality of intubating conditions was assessed. Excellent or good conditions were considered to be acceptable intubating conditions, whereas fair and poor conditions were considered unacceptable.

Results: Mean age, weight, gender distribution, and ASA grades were comparable in both groups. The overall quality of intubation was found to be better in group S than in group R, and the difference was statistically significant (p=0.004). The duration of action was significantly longer in group R than in group S (p<0.001). Hemodynamic stability was comparable in both the groups, except for heart rate at 10 min, which was higher in Group R than in Group S. Incidence of fasciculation was significantly more in Group S as compared to Group R, and the difference was found to be highly significant (p=0.0001).

Conclusion: Succinylcholine for rapid sequence intubation is associated with better intubation conditions than rocuronium.

Keywords: Intubation, muscle relaxant, rocuronium, succinylcholine

Introduction

Rapid and safe endotracheal intubation is paramount importance in practice of general anesthesia. Adequate intubating conditions are required to avoid airway trauma and adverse sympathetic responses. With advent of muscle relaxation, anesthesia practice changed drastically for better. First muscle relaxant for surgery, d-tubocurarine, was introduced in 1942.[1] With this relaxant, jaw relaxation could easily be obtained to facilitate orotracheal intubation. This invention soon inspired R.R. Macintosh to invent the famous Macintosh laryngoscope in 1943.[2] Although d-tubocurarine could produce jaw relaxation to facilitate orotracheal and nasotracheal intubation, it brought with it, its own drawback. It produced muscarinic block and ganglion block leading to tachycardia and hypotension.[3] The onset of action was also delayed taking up to 3 minutes to produce good intubating condition. This created a problem in emergency cases and full stomach cases where rapid procurement of airway is the priority to avoid regurgitation and aspiration. Soon after in

1954 studies have reported manifold increase in mortality in patients receiving dTC than who had not received muscle relaxation thereby underlining the risks involved in using muscle relaxants for intubation.[4] Succinyl choline has been famous muscle relaxant available for rapid sequence induction of anesthesia where, securing the airway quickly, such as in cases with full stomach requiring emergency surgeries, was of critical importance.[5] However, the use of depolarizing muscle agents such as succinylcholine was found to be associated with risk of hyperkalemia, variable increase in intracranial pressure and intraocular pressure. Moreover, succinyl choline is contraindicated in patients with burns, crush injuries, muscular dystrophies, severe abdominal sepsis, denervation syndrome, malignant hyperthermia or allergy to succinyl choline in susceptible patients and development of phase II block after a large dose or continuous infusion. The duration of succinylcholine chloride was prolonged in patients with pseudo cholinesterase deficiency. All these conditions where use of succinyl choline is contraindicated has led scientists to look for newer drug which can be used as an alternative to succinyl choline.[6] In 1967 the studies first reported on clinical administration of the synthetic amino steroid pancuronium. Development of the intermediate-acting neuromuscular blocker built on the compound's metabolism and resulted in the introduction of vecuronium, an amino steroid which is also a mono-quaternary analogue of pancuronium and atracurium which is a benzylisoquinolinium, into clinical practice in the 1980s but none of these nondepolarizing muscle relaxants could be match succinyl choline with respect to onset of action.[7] Although various methods, such as the use of the "priming" (divided dose) technique and the use of larger doses of atracurium and vecuronium, have been tried in an attempt to reduce the onset time of these neuromuscular blockers, these methods have either proved unsuccessful or hazardous to the patient, as in the case of the priming technique, or resulted in a long duration of action as with the use of larger doses. In 1990 a new non depolarizing muscle relaxant, Rocuronium Bromide which challenged the onset time of Succinyl choline facilitating safe and rapid endotracheal intubation was introduced.[8] Rocuronium bromide is safe as there are no side effects like histamine release unlike other non-depolarizing muscle relaxants, maintains cardiovascular stability and is known for rapid recovery. Also, it provides intubating conditions similar to those of succinyl choline 60 to 90s after administration. Dose of rocuronium usually defines the onset time, duration and intubating conditions. The study was undertaken to evaluate the quality of intubating conditions with rocuronium bromide and to compare it with that of succinylcholine for use during general anesthesia in adult patients.

Methods

This was a comparative study conducted in the department of anesthesiology of a tertiary care medical college in Maharashtra, India. The duration of study was 2 years from January 2021 to December 2022. 60 patients undergoing various surgeries, such as Laparoscopic appendectomy, Laparoscopic cholecystectomy, modified radical mastectomy, tonsillectomy and Laparoscopic ovarian cystectomy, under general anesthesia were included in this study. The institutional ethical committee approved the study. The patients who were undergoing elective surgeries under general anesthesia and having ASA Grades I and II and Mallampati score of I and II were included. Patients who refused consent, those with Mallampati score of I and II as well as patients with ASA grade III and above were excluded from the study. Those with known allergies to anesthetic drugs and having serious comorbid conditions were also excluded from the study. Institutional ethical committee approved the study and written informed consent was obtained from all the participants. The sample size was calculated on the basis of pilot study done by Panda *et al.* assuming 90% power and 95% confidence interval, the sample size required was 19 patients per arm (total 38). Based on central limit theorem, sample size was determined to be enough if it was more than 25 thus, 30 patients were included in each group. Computer based randomization was used for randomization and anesthetists were blind to allocation information. Group S: received Succinylcholine 1.5mg/kg intravenously. Group R: received Rocuronium bromide 0.6mg/kg intravenously. All patients were thoroughly evaluated and intravenous cannula was secured with 20G IV line. Patients were shifted to operating room and IV fluids were started. Continuous monitoring of patients for heart rate, systolic and diastolic blood pressures, ECG, SPO2 and ETCO2 was also started. Patients were premedicated

with Inj. Glycopyrrolate 4 mcg /kg IV, Inj. Midazolam0.05mg/kg IV and Fentanyl 2mcg/kg. Preoxygenation of 3 minutes was followed by induction with Inj. Propofol 2mg/kg IV Both drugs, either rocuronium bromide (Group R) or succinyl choline (Group S) were given to patients depending upon the group to which they belonged. Surgery commenced at 60 seconds in every patient. Patients were intubated with cuffed endotracheal tube no. 7.0/8.0. In all patients quality of intubating conditions was assessed by using Cooper *et al.*[9] scoring system.The intubating conditions were divided into excellent (Jaw relaxed, vocal cords apart and immobile, no diaphragmatic movements), good (Jaw relaxed, vocal cords apart and immobile, some diaphragmatic movements), fair (Jaw relaxed, vocal cords moving, "bucking") or poor (Jaw not relaxed; vocal cords closed). Excellent or good conditions were considered acceptable whereas poor and inadequate conditions were considered unacceptable intubating conditions. Anesthesia was maintained with oxygen, nitrous oxide (33:67), isoflurane and intermittent positive pressure ventilation. Hemodynamic stability was assessed my continuous monitoring of HR, mean arterial pressure and saturation preoperatively and then immediately after intubation and 10 min, 20 min, 30 min and 40 min after intubation. Side effects such as tachycardia, bradycardia, arrhythmia, histamine release, and laryngospasm and muscle fasciculation's were noted in all the cases. Duration of action of muscle relaxants was considered to be extending until recovery of spontaneous respiration. At the end of the procedure patients were reversed with neostigmine 0.04 mg/kg and Glycopyrrolate 0.005 mg/kg titrated to response and the patient was extubated. SPSS 23.0 was used for data analysis. Descriptive statistics were elaborated in the form of means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Group comparisons made using independent sample t-test for continuously distributed data, and chi-square test for categorical data. Repeated observations were compared using paired t-test or repeated measures ANOVA as applicable. P value less than 0.05 was taken as statistically significant.

Result

The groups were compared for mean age, weight, Gender distribution and ASA Grades. The mean age of cases in group R and group S was found to be 35.12 +/- 7.46 and 32.34 +/- 6.98 years respectively. The mean weight of patients in group R and S was found to be 62.34 +/- 7.86 kg and 60.12 +/- 6.98 kg respectively. The mean age, weight as well as gender distribution and ASA grades were found to be comparable in both the groups with no statistically significant difference in any of these parameters in both the groups. Mallampati classification score of both the groups were also found to be comparable in both the groups with no statistically significant difference (p>0.05; Table 1).

The most common surgery performed in group R was laparoscopic appendectomy (33.33%) whereas the most common surgery in group S was laparoscopic cholecystectomy (36.67%). Overall the most common surgery was laparoscopic cholecystectomy (33.33%) followed by laparoscopic cholecystectomy (31.67%). The other surgeries undertaken were Laparoscopic ovarian cystectomy (13.33%), tonsillectomy (11.67%), and Modified radical mastectomy (10%) (Fig. 1).

Comparison of quality of intubating

Table 1 Comparison of Mean Age, Weight, Gender, ASA and MPC Grades in Patients

		Group R	Group S	P Value
Mean Age		35.12 +/- 7.46	32.34 +/- 6.98	0.079
Gender Distribution	Males	22 (73.33%)	17 (56.7%)	0.279
	Females	8 (26.66%)	13 (43.3%)	
Weight		62.34 +/- 7.86	60.12 +/- 6.98	0.079
ASA Grade	Grade I	22 (73.33%)	24 (80 %)	0.902
	Grade II	8 (26.66%)	6 (20%)	
MPC Grade	MPC I	16 (53.33%)	21 (70%)	0.288
	MPC II	14 (46.66%)	9 (30%)	

Comparative Evaluation of Effectiveness of Rocuronium Bromide vs. Succinyl Choline on Quality of Intubating Conditions during General Anesthesia

Table 2 Comparison of Quality of Intubating Conditions in Studied Cases

		Group			Fisher's Exact Test	
		R (n=30)	S (n=30)	Total (n=60)	χ2	P Value
Jaw Relaxation	Score 0	0	0	0	-	-
	Score 1	0	0	0	-	-
	Score 2	5 (16.7%)	0 (0.0%)	5 (8.3%)	5.455	0.052
	Score 3	25 (83.3%)	30 (100.0%)	55 (91.7%)		
Vocal Cord Position	Score 0	0	0	0		
	Score 1	4 (13.3%)	0 (0.0%)	4 (6.7%)	13.098	<0.001
	Score 2	13 (43.3%)	4 (13.3%)	17 (28.3%)		
	Score 3	13 (43.3%)	26 (86.7%)	39 (65.0%)		
Intubation Response	Score 0	0	0	0		
	Score 1	6 (20.0%)	0 (0.0%)	6 (10.0%)	8.182	0.012
	Score 2	12 (40.0%)	10 (33.3%)	22 (36.7%)		
	Score 3	12 (40.0%)	20 (66.7%)	32 (53.3%)		

conditions in both the groups showed that better jaw relaxation was seen in Group S as compared to Group R however this difference was not found to be statistically significant. However, the analysis of 2 other parameters namely vocal cord position and intubation response showed that both of these parameters were better in Group S as compared to Group R and the difference was statistically significant (p<0.05; Table 2).

Comparison of both the groups on the basis of total score for quality of intubation showed that mean total score in Group R and Group S was 7.33 +/- 1.37 and 8.50 +/- 0.68 respectively. Group S was having a better total score as compared to Group R and the difference between the 2 groups in terms of Total Score was found to be significant (W=222.000, p=<0.001) The analysis of patients in both the groups on the basis of duration of action (in minutes) of muscle relaxants showed that the mean duration of action in group R and group S was 22.93 +/- 5.45 and 11.97 +/- 1.71 respectively. The duration of action was longer in group R as compared to group S and the difference was significant (p<0.001; Table 3).

The comparison of both the groups on the basis of quality of intubation showed that most of the patients in Group S had excellent

Table 3 Comparison of Mean Score of Quality of Intubation and Duration of Action in Both the Groups

| Mean Score of Quality of Intubation and Duration of Action		Group			Wilcoxon-Mann- Whitney U Test	
		R	S	W	p value	
Mean Score of Quality of Intubation	Mean (SD)	7.33 +/- 1.37	8.50 +/- 0.68			
	Median (IQR)	8 (6-8)	9 (8-9)	222.000	<0.001	
	Range	5–9	7–9			
Duration of Action (Minutes)	Mean (SD)	22.93 +/- 5.45	11.97 +/- 1.71			
	Median (IQR)	22 (18.25–25)	12 (11–13)	899.000	<0.001	
	Range	15–38	7–15			

Table 4 Comparison of Groups on the Basis of Overall Quality of Intubation and Acceptable Grades

Overall Quality of intubation and acceptable grades		Group			Fisher's Exact Test	
		R (n=30)	S (n=30)	Total (n=60)	χ^2	P Value
Overall Quality of Intubation	Excellent	16 (53.3%)	27 (90.0%)	43 (71.7%)	10.583	0.004
	Good	10 (33.3%)	3 (10.0%)	13 (21.7%)		
	Fair	4 (13.3%)	0 (0.0%)	4 (6.7%)		
Acceptable Grades	Yes	26 (86.7%)	30 (100.0%)	56 (93.3%)	4.286	0.112
	No	4 (13.3%)	0 (0.0%)	4 (6.7%)		

quality of intubation (90%) whereas good and fair quality was seen in 13 (21.7%) and 4 (6.7%) patients respectively. In group R excellent quality of intubation was seen in 16 (53.3%) patients. Overall quality of intubation was found to be better in group S as compared to group R and the difference was statistically significant (P=0.004). Fisher's exact test was used to explore the association between 'Group' and 'Acceptable Grade'. In group R 26 (86.7%) patients had acceptable grades whereas in group S all 30 (100%) patients were found to have acceptable grades. Though comparatively less patients had acceptable grades in group R as compared to group S however the difference between the groups in terms of distribution of Acceptable Grade was not found to be significant (χ^2=4.286, p=0.112) (Table 4).

Both the groups were compared for heart rate, mean arterial pressure and SPO2 pre-operatively and postoperatively and till 12 hours. The heart rate was found to be comparable at all the times except 15 minutes (P<0.05). Mean arterial pressure and SPO2 were found to be comparable in both the groups at all the times with no statistically significant difference at any point in time (p>0.05; Table 5).

The analysis of side effects in both the groups and their comparison showed that in group R 28 (93.33%) patients didn't have any adverse effects while 2 (6.66%) patients developed tachycardia. In group S 1 (3.33%) patient developed bradycardia. Muscle fasciculation's were seen in 24 (80%) of the patients in group S whereas no patient in Group R developed fasciculation's. Incidence
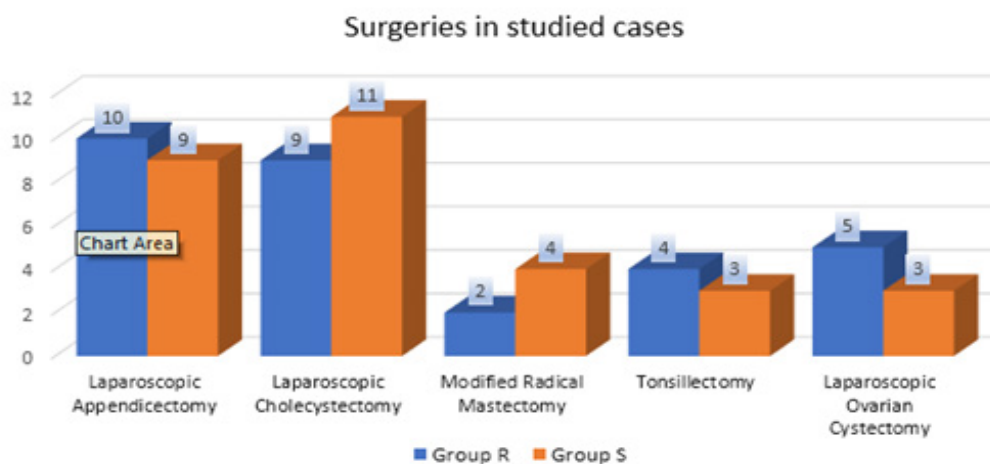
Fig. 1 Types of Surgeries in Studied Cases

Table 5 Comparison of Mean Heart Rate, Mean Arterial Pressure and SPO$_2$

Heart Rate(BPM)		Group		P value (Wilcoxon-Mann- Whitney Test)
		Group R Mean (SD)	Group S Mean (SD)	
Heart Rate (BPM)	0 Min	84.12 +/- 8.98	82.36 +/- 8.12	p>0.05
	15 Min	86.28 +/- 9.12	76.42 +/- 8.34	p=0.0001
	30 Min	84.30 +/- 9.80	86.34 +/- 9.12	p>0.05
	1 Hr	82.07 +/- 9.04	84. 36 +/- 9.90	p>0.05
	2 Hr	83.74 +/- 8.18	82.46 +/- 8.86	p>0.05
	3 Hr	81.83 +/- 10.12	84.62+/- 8.12	p>0.05
	4 Hr	80.12 +/- 9.90	82.42 +/- 7.98	p>0.05
	5 Hr	82.86 +/- 10.12	84.34 +/- 8.84	p>0.05
	6 Hr	80.46 +/- 9.70	80.12 +/- 9.12	p>0.05
	7 Hr	78.34 +/- 9.34	80.34 +/- 8.12	p>0.05
	8 Hr	82.30 +/- 10.30	78.64 +/- 6.34	p>0.05
	9 Hr	84.12 +/- 6.82	82.34 +/- 6.58	p>0.05
	10 Hr	80.34 +/- 5.54	82.66 +/- 7.14	p>0.05
	11 Hr	78.54 +/- 6.12	80.12 +/- 6.78	p>0.05
	12 Hr	76.86 +/- 5.90	78.34 +/- 7.10	p>0.05
Mean Arterial Pressure	0 Min	90.92 +/- 8.34	89.03 +/- 8.10	p>0.05
	15 Min	92.34 +/- 8.24	96.87 +/- 10.24	p>0.05
	30 Min	96.96 +/- 9.12	93.37 +/- 9.48	p>0.05
	1 Hr	94.34 +/- 8.48	92.50 +/- 8.68	p>0.05
	2 Hr	96.24 +/- 9.34	91.70 +/- 7.78	p>0.05
	3 Hr	95.34 +/- 8.34	90.73 +/- 7.24	p>0.05
	4 Hr	92.20 +/- 9.84	94.40 +/- 8.12	p>0.05
	5 Hr	90.94 +/- 8.86	88.68 +/- 8.34	p>0.05
	6 Hr	88.34 +/- 9.12	86.34 +/- 9.12	p>0.05
	7 Hr	86.68 +/- 9.34	84.68 +/- 9.02	p>0.05
	8 Hr	88.54 +/- 9.12	90.34 +/- 10.34	p>0.05
	9 Hr	92.34 +/- 9.46	92.46 +/- 8.98	p>0.05
	10 Hr	90.86 +/- 8.24	90.34 +/- 9.46	p>0.05
	11 Hr	91.34 +/- 9.12	90.48 +/- 10.02	p>0.05
	12 Hr	90.56 +/- 9.02	88.62 +/- 9.90	p >0.05
Spo2	0 Min	99.6 +/- 0.48	99.4 +/- 0.86	p>0.05
	15 Min	99.4 +/- 0.86	99.54 +/- 0.74	p>0.05
	30 Min	99.6 +/- 0.48	99.60 +/- 0.48	p>0.05
	1 Hr	99.6+/- 0.48	99.20 +/- 0.72	p>0.05
	2 Hr	99.4 +/- 0.86	99.60 +/- 0.48	p>0.05
	3 Hr	99.2 +/- 0.74	99.40 +/- 0.86	p>0.05
	4 Hr	99.6 +/- 0.48	99.60 +/- 0.48	p>0.05

Table 5 (Continued)

Heart Rate(BPM)		Group		P value (Wilcoxon-Mann- Whitney Test)
		Group R Mean (SD)	**Group S** Mean (SD)	
Spo2	5 Hr	99.0 +/- 0.98	99.4 +/- 0.86	p>0.05
	6 Hr	98.80 +/- 1.12	99.2 +/- 0.74	p>0.05
	7 Hr	99.40 +/- 0.86	99.40 +/- 0.86	p>0.05
	8 Hr	99.60 +/- 0.48	98.12 +/- 0.74	p>0.05
	9 Hr	99.40 +/- 0.86	99.40 +/- 0.86	p>0.05
	10 Hr	99.60 +/- 0.48	99.60 +/- 0.48	p>0.05
	11 Hr	99.40 +/- 0.86	99.46 +/- 0. 46	p>0.05
	12 Hr	99.60 +/- 0.48	99. 34 +/- 0.84	p>0.05

of fasciculation was significantly more in group S as compared to Group R and the difference was found to be highly significant (P=0.0001). Other side effects were comparable in both the groups.

Discussion

Rapid and safe endotracheal intubation is of paramount importance in practice of general anesthesia. The only muscle relaxant famous for its rapid onset of action was succinyl choline until the discovery of rocuronium bromide. The quest to find alternative to succinyl choline has led scientist to look for new drug and that's when rocuronium bromide, non-depolarizing muscle relaxant became famous for its comparable time of onset of action.[10] The newer drug also helped to overcome the side effects which were associated with succinyl choline like bradycardia, arrhythmias, hyperkalemia, variable increase in intraocular, intragastric and intracranial pressures. To compare the effectiveness of Rocuronium Bromide and Succinyl Choline, intubating conditions were assessed in this study. In this study Comparison of quality of intubating conditions showed that vocal cord position and intubation response showed that both of these parameters were better in Group S as compared to Group R and the difference was statistically significant (p<0.05). Tran DT *et al* conducted an extensive literature review to determine whether rocuronium creates intubating conditions comparable to those of succinylcholine during RSI intubation.[11] For this purpose the authors reviewed 37 randomized controlled trials (RCTs) or controlled clinical trials (CCTs) relating to the use of rocuronium and succinylcholine. The study found that Overall, succinylcholine was superior to rocuronium for achieving excellent intubating conditions: RR 0.86 (95% confidence interval (CI) 0.81 to 0.92; n = 4151) and clinically acceptable intubation conditions (RR 0.97, 95% CI 0.95 to 0.99; n = 3992, 48 trials). On the basis of these findings the authors concluded that Succinylcholine created superior intubation conditions to rocuronium in achieving excellent and clinically acceptable intubating conditions. Similar findings were also reported by the authors such as Guihard B *et al*[12] and Chavan SG *et al*.[13] The analysis of patients in both the groups on the basis of duration of action of muscle relaxants showed that the mean duration of action in group R and group S was 22.93 +/- 5.45 and 11.97 +/- 1.71 minutes respectively. The duration of action was longer in group R as compared to group S and the difference was highly significant (p<0.001). Magorian T *et al* undertook a study to compare rocuronium, succinylcholine, and vecuronium for rapid-sequence induction of anesthesia in adult patients.[14] For this purpose Fifty patients, ASA 1-3, were randomly designated to receive one of three intravenous doses of rocuronium (0.6, 0.9, and 1.2 mg/kg), vecuronium (0.1 mg/kg), or succinylcholine (1.0 mg/kg). The time from injection of muscle relaxant until complete ablation of T1 (onset) and recovery of T1 to 25% (duration) were recorded. The study found that Clinical duration of action was longest with 1.2 mg/kg rocuronium, similar with 0.6 and 0.9 mg/kg rocuronium, and vecuronium, and least with succinylcholine. These findings were similar to findings of ours

study. Similar findings were also reported by the authors such as Li G et al.[15] and Sparr HJ et al.[16] The comparison of hemodynamic parameters in both the groups showed that the heart rate was found to be comparable at all the times except 10 minutes (p<0.05). Mean arterial pressure and SPO2 were found to be comparable in both the groups at all the times with no statistically significant difference at any point in time (p>0.05). Lenin et al.[17] undertook a study to compare the onset time, duration of action, intubating condition and hemodynamic effect of rocuronium bromide at the dose of 0.8 mg/kg and Succinylcholine at the dose of 1.5 mg/kg.The study found that both the drugs raised mean Heart rate, Systolic Blood Pressure, Diastolic Blood pressure, MAP from intubation to subsequent intervals however this increase was comparable with no statistically significant difference between the groups. Similar hemodynamic comparability

between succinylcholine and rocuronium was also reported by the authors such as Sorensen et al.[18] and Li et al.[19] The analysis of cases on the basis of adverse effects showed that Incidence of fasciculation was significantly more in group S as compared to Group R and the difference was found to be highly significant (p=0.0001). Other side effects were comparable in both the groups. 24 (80%) patients in group S were found to have muscle fasciculation's whereas no patient in group R had fasciculations. Similar findings were also reported by Zhang et al.[20]

Small number of cases and use of fixed dose of rocuronium were the limitations of our study. A similar study with larger cohort will further substantiate the findings of our study. In conclusion use of succinylcholine for rapid sequence intubation was found to be associated with better intubation conditions as compared to rocuronium.

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Thyroid Profile and Serum Lipid Level in Women with Normal Pregnancy

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Abstract

Objective: To evaluate the changes in thyroid profile and serum lipid level in normal pregnancy.

Methods: This observational study was conducted at the Department of Biochemistry of Santosh Medical College, Ghaziabad, UP, India, from June 2021 to February 2022. In this study, 200 average pregnant women were enrolled. The thyroid profile was estimated using the ELISA method, and the lipid profile was measured using the enzymatic kit method. All data were expressed as means and standard deviations, and SPSS version 17 was used for statistical analysis.

Results: This observational study observed that the mean T3, T4, and TSH levels increased significantly in the second trimester compared to the first trimester. In contrast, the mean value of T3, T4, and TSH decreased in the third trimester as compared to the second trimester. The mean levels of total cholesterol, triglyceride, and LDL-cholesterol increased significantly, while the mean value of HDL-cholesterol decreased significantly in the second and third trimesters when compared to the first trimester.

Conclusion: This study demonstrated abnormal lipid and thyroid metabolism. Changes in thyroid profile may be associated with adverse obstetric outcomes. The altered lipid parameters, mainly High TG and low HDL-C concentrations, may promote vascular dysfunction and oxidative stress.

Keywords: Pregnancy, thyroid hormones, triglycerides, trimester

Introduction

Pregnancy is known as period of gestation. During this period new life grows inside a female's uterus. Pregnancy causes alteration in internal and external physiological status of female. Many external physiological changes are seen in this time, such as changes in blood values which may appear pathological in non-pregnant women. However these changes during pregnancy are beneficial for development and growth of fetus. Therefore this altered physiology has great impact and helps to supply proper nutrients and protection to developing fetus until delivery.[1] These changes are also due to the many endocrinal change occurs in pregnancy. In this thyroid gland has critical role which regulates the thyroid hormones synthesis that is necessary for the infant's brain and nervous system development. Since the fetus completely depends on the mother's thyroid hormone throughout the first trimester, the mother's thyroid gland is enlarged to produce more thyroid hormone. Dysfunction in thyroid gland is also common during pregnancy. If these are remained untreated then causes many reverse effects on pregnancy and fetal

outcomes.[2] During pregnancy, the mother physically changes, and the increased blood levels of progesterone, estrogens, and pancreatic beta-cell hyperplasia change the mother's metabolic milieu. A significant part of the lipid profile's disturbance is due to insulin resistance and ovaries-estrogens (in women). So identification of these disorders and their treatment are necessary to prevent complications related to pregnancy. Changes in thyroid hormones and in TSH may be a factor in a disrupted lipid profile, particularly in the third trimester. Many studies have been examine the alterations in a pregnant woman's lipid profile, T3, T4, and TSH during their three stages of pregnancy to ascertain why these characteristics change during pregnancy.[3] Reports on the relationship between dyslipidemia and pregnancy outcomes and thyroid gland malfunction have produced conflicting results and also the first trimester receives less attention in research, which tends to concentrate on the late stages of pregnancy. Hence this study was aimed to determine serum lipid level and thyroid profile in all trimester of normal pregnancy.

Methods

This research was conducted at the Santosh Medical College in Ghaziabad, Uttar Pradesh, in the Department of Biochemistry, India from June 2021 to February 2022. Institutional ethical committee clearance [SU/2020/536(50)] and inform consent from patient were taken prior to the study. This study included 200 pregnant healthy women with 21–32 years of age. In this study, healthy pregnant women with age more than 20 years were included. Women on hormonal

therapy, steroid therapy, already diagnosed thyroid patients, women having abnormal liver function and kidney function and women having acute or chronic inflammatory disease were excluded. Blood sample were collected after 8-12 hours fasting three times from the women in first, second and third trimester in fluoride/Plain vials under all aseptic precautions. Plasma/ serum were separated and all the parameters were measured on the day of collection. Fasting blood glucose, total cholesterol, HDL-cholesterol, triglyceride and LDL-cholesterol were measured by enzymatic kit method by Fully Automatic analyzer (Beckman Coulter- AU-480). Serum T3, T4 and TSH were done by commercially available ELISA kits by Beckman Coulter-Chemistry Analyzer Access-2. Blood glucose and lipid parameters were measured by using fully automated analyzer (Beckman Coulter –AU-480). Chemistry Analyzer-Access-2's (automated analyzer) was used to measure the thyroid profile. Statistical Package for Social Sciences (SPSS) version 17 was used to conduct the statistical analysis. The results were summarized as mean and standard deviation in several tables. The confidence intervals for each of the presented p-values were determined at the 95% level. P < 0.05 was considered significant.

Results

This study included 200 normal pregnant women of more than 20 year of age. The mean value of T3 and TSH increases in 2nd and 3rd trimester of pregnancy as compared to 1st trimester and it was statistically significant. The mean value of T4 increases in 2nd trimester but decreases in 3rd trimester and it was

Table 1 Showing Comparison of Biochemical Parameters in 1st and 2nd Trimester of Pregnancy (n=200)

Variables	1st Trimester	2nd Trimester	p-value
T3 (ng/mL)	1.07 ± 0.15	1.19 ± 0.27	0.038
T4 (µg/mL)	5.54 ± 2.06	7.56 ± 2.11	0.004
TSH (µIU/mL)	1.76 ± 0.74	3.97 ± 1.96	<0.0001
Fasting blood Glucose (mg/dL)	81.03 ± 11.89	90.43 ± 15.42	0.01
Total Cholesterol (mg/dL)	155.73 ± 27.61	171.8 ± 30.11	0.035
HDL-cholesterol (mg/dL)	49.67 ± 5.05	46.20 ± 5.80	0.016
Triglyceride (mg/dL)	154.83 ± 26.02	186.30 ± 32.38	0.0001
LDL-cholesterol (mg/dL)	72.10 ± 8.43	85.23 ± 11.23	<0.0001

*p-value less than 0.05 considered as statistically significant

Table 2 Showing Comparison Of Biochemical Parameters in 1st and 3rd trimester of Pregnancy (n=200)

Variables	1st Trimester	3rd Trimester	p-value
T3 (ng/mL)	1.07 ± 0.15	1.32 ± 0.17	<0.0001
T4 (µg/mL)	5.54 ± 2.06	6.58 ± 1.06	=0.017
TSH (µlU/mL)	1.76 ± 0.74	4.87 ± 1.45	<0.0001
Fasting blood Glucose (mg/dL)	81.03 ± 11.89	97.12 ± 8.78	<0.0001
Total Cholesterol (mg/dL)	155.73 ± 27.61	194.10 ± 44.33	=0.0002
HDL-cholesterol (mg/dL)	49.67 ± 5.05	41.87 ± 4.50	=0.0001
Triglyceride (mg/dL)	154.83 ± 26.02	208.7 ± 47.71	<0.0001
LDL-cholesterol (mg/dL)	72.10 ± 8.43	111.45 ± 18.91	<0.0001

*p-value less than 0.05 considered as statistically significant

statistically significant. The mean value of total cholesterol, triglyceride and LDL-cholesterol were found to be increased significantly in 2nd and 3rd trimester as compared to 1st trimester and the mean value of HDL-cholesterol decreases significantly in 2nd and 3rd trimester as compared to 1st trimester (Table 1 and 2).

The differences in all the studied parameters in 2nd and 3rd trimester were statistically significant (Table 3).

Discussion

Pregnancy is one of the most vital phases in women life in which many hormonal, immunologic, vascular, metabolic and psychological changes are seen. These changes are beneficial to nurture the developing fetus. These changes also impact on level of normal biochemical parameters while others may mimic symptoms of medical disease. In current study total 200 pregnant women were taken and were followed up in their all three trimesters. Maximum women were from 20 to 30 age group which was line with previous study that states that the most probable fertile years and reproductive age of woman is 20–30 years and her best reproductive years are in 20s.[4] Lipid profile is significantly affected by the endogenous sex hormones of females. Endocrine changes during pregnancy (e.g., rising levels of estrogen, progesterone, and cortisol) cause lipogenesis and accumulation of fat associated with hyperphagia. Pregnancy-related increases in lipid synthesis are required as an energy source to meet the metabolic requirements of both the mother and the foetus.[4] In present study, the mean value of total cholesterol, Triglyceride and LDL-cholesterol in first trimester, second trimester and third trimester of pregnancy were found to be increased significantly. These results were line with the previous studies that reported gradually increase of lipid fractions during in

Table 3 showing comparison of biochemical parameters in 2nd and 3rd trimester of pregnancy (n=200)

Variables	2nd Trimester	3rd Trimester	p-value
T3 (ng/mL)	1.19 ± 0.27	1.32 ± 0.17	0.295
T4 (µg/mL)	7.56 ± 2.11	6.58 ± 1.06	0.03
TSH (µlU/mL)	3.97 ± 1.96	4.87 ± 1.45	0.047
Fasting blood Glucose (mg/dL)	90.43 ± 15.42	97.12 ± 8.78	0.04
Total Cholesterol (mg/dL)	171.8 ± 30.11	194.10 ± 44.33	0.026
HDL-cholesterol (mg/dL)	46.20 ± 5.80	41.87 ± 4.50	0.002
Triglyceride (mg/dL)	186.30 ± 32.38	208.7 ± 47.71	0.037
LDL-cholesterol (mg/dL)	85.23 ± 11.23	111.45 ± 18.91	<0.0001

*p-value less than 0.05 considered as statistically significant

all three stages of pregnancy.[4,5]Another related reported the gradually increase mean value of cholesterol and triglycerides in second and third trimester which is similar to the present study.[4] Kumari et.al. in their study reported significant increase in that cholesterol during all three trimester.[6] Other study also showed that TC and TG concentration rise up in late pregnancy compared with non-pregnant women.[7] Evidence also suggests that blood lipids return to pre-pregnancy levels after delivery which recommends that the elevated serum lipids may have significant role in fetal development. However high cholesterol level during pregnancy may lead to pregnancy induced hypertension, cardiovascular risk which can threaten the life of both the mother and child. On the other way, low cholesterol can lead to early and premature labor and low birth weight.[8]

One study that also reported hypertriglyceridemia in pregnancy and reported gradually increased level of TG during trimester and also found significant difference when compared with non-pregnant women.[9] For this explanation, one study stated that due to high energy demand in pregnancy maternal need of fuel switch from carbohydrate to lipid metabolism for energy production. Therefore, in early pregnancy there is seen increased lipid deposition and decreased lipolysis.[4] Another explanation of rise in triglyceride and other lipid components during normal pregnancy are seen in parallel with the rise in gestational age which was observed with the rise in estrogen and progesterone level during gestational period.[4,9]Decreased pattern in HDL-C was found in this study. Low HDL-C levels are said to increase the risk of coronary heart disease, and many pregnancies have had mixed outcomes. It is thought that the fall in serum HDL-C during the third trimester of a typical pregnancy may be a potential risk factor for atherosclerosis. Another explanation of increased LDL-C is high levels of progesterone and estrogen during pregnancy.[4] The higher LDL-c pattern during pregnancy may be utilized to identify women who may experience atherogenic alterations in the future.[10] Similar pattern of variations in lipid profile was also presented by other previous studies as found in present study.[4,10] A study stated that there may be two factors for rise in TG, first increased activity of hepatic lipase, which is responsible for the synthesis of hepatic triglycerides; and reduced lipoprotein lipase activity, which results in a reduction in the catabolism of adipose tissues.[10] During

pregnancy significant changes are also seen in thyroid hormone physiology and thyroid gland anatomy.[10]

In present study elevated pattern in TSH level was observed in first, second and third phase of pregnancy respectively. However, it was observed in normal limit, but increasing TSH value indicates towards the risk for developing hypothyroidism. In support with this Yoganathan et.al., studied on thyroid status in pregnant women and found increased TSH value in pregnant women with hypothyroidism and showed positive correlation.[11] Another study of Mehta *et al.*,[12] reported increased TSH concentration in third trimester compared with second trimester.Study stated that raised TSH value may be considered as a risk factor of decreased neurological development and preterm birth.[13]In the present study, the mean T3 level was increase significantly in 2nd and 3rd trimester as compared to 1st trimester but it was in normal range. T4 level were increase in 2nd trimester as compared to 1st trimester but decreases in 3rd trimester as compared to 2nd trimester. Iodine is organized and oxidized by the thyroid peroxidase enzyme, which also produces the hormones fT4 and fT3.[14] A glycoprotein called thyroglobulin serves as a substrate for the production and storage of thyroid hormones.[15] Hypothyroidism is the outcome of both antibodies in autoimmune thyroid diseases. Thyroid autoimmunity is linked to recurrent miscarriage, which is probably brought on by generalized immune system activation and trans placental transfer of antibodies that result in fetal rejection.[16]

Females are high risk on thyroid dysfunction. Hypothyroidism is linked with increased lipid fraction i.e. TC, LDL, TG and decreased HDL-C. Elevated level of LDL-C results in increased in oxidation of LDL-C which is high risk factor of atherosclerosis. Hypothyroidism is also linked with decreased activity of lipoprotein lipase which leads to decreased clearance of TG rich lipoprotein.[17] Line with present study Sangeeta et.al, also reported elevated levels of TC, LDL-C and TG with elevated level of TSH. Decreased HDL-C is also linked with hypothyroidism due to increased transfer of cholesterol esters from HDL to VLDL mediated through CETP, which effect on increased HDL catabolism.[18] Thyroid profile and lipid profile both have vital role in female pregnancy. In early pregnancy, thyroid impairment was common and prevalent and associated with dyslipidemia. During pregnancy, a poor metabolic phenotype is associated with thyroid dysfunction. Effect of

body weight on association of lipid parameters and thyroid hormones are not studied well. A woman's physiological weight increase during pregnancy may have an impact on her lipid profile and thyroid hormone levels. A bigger sample size and prospective methodological investigations in different centers are required in the future to examine the association of thyroid profile with lipid profile with a larger sample size as the current study was only done in one hospital.

In the present study, it was observed that T3, T4 and TSH levels were raised. Obstetric problems can result from aberrant thyroid hormones. Thyroid disorder has an impact on both the mother and the fetus. Early in pregnancy, maternal thyroid hormones and TSH are linked to dyslipidemia and a number of unfavorable pregnancy outcomes. Total Cholesterol, Triglycerides, and LDL were shown to have significantly higher levels across all lipid profile indicators as a result of endothelial dysfunction. Conventional screening of maternal thyroid in early pregnancy may help improve lipid levels and decrease several adverse pregnancy outcomes.

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Outcome of Posterior Cruciate Ligament Avulsion Fractures from Tibial Attachment Treated by Open Reduction and Internal Fixation

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Abstract

Objective: To study the clinical profile and treatment outcome of mucormycosis associated with the second wave of COVID-19 pandemic.

Methods: An observational study was conducted in a tertiary care center over a period of 12 months, including a 6-month post treatment follow up. Study included all COVID positive patients with a clinical and radiological evidence of rhino-orbito-cerebral mucormycosis during the second wave of COVID-19. All patients underwent further diagnostic workup and confirmed cases underwent surgical debridement and Amphotericin B was started.

Results: A total of 59 patients presented with mucormycosis with the mean age being 52.7 years and unilateral facial and orbital edema as the most common symptoms (28.8%). All were diabetic with HbA1c >7 in 54.2%. The mean duration of presentation was 20.7±7.9 days from the onset of COVID-19 infection. Unilateral involvement of the paranasal sinuses was the most common finding in MRI. Early administration of Amphotericin B with prompt surgical debridement was performed in all cases. Orbital exenteration was conducted in nine patients for better fungal load clearance. Patients showed a good response to surgical debridement and prompt medical treatment, with a mortality rate of 27%.

Conclusion: COVID-19 associated mucormycosis is difficult to treat and often presents in late stage. Uncontrolled diabetes, immunocompromised state, and steroid-induced immunosuppression were important risk factors. A close surveillance for early identification and initiation of treatment is mandatory. Repeated surgical debridement to clear the dead tissue is effective to control fungal load.

Keywords: Amphotericin B, COVID-19, invasive fungal sinusitis, mucormycosis

Introduction

The Posterior Cruciate Ligament (PCL) is stronger than anterior cruciate ligament (ACL) and plays a crucial role in stabilizing the knee.[1] It acts as a primary restraint against posterior tibial displacement and works in conjunction with the anterior cruciate ligament (ACL) to regulate external rotation of the knee during extension. PCL injuries are estimated to account for approximately 20% of knee ligament injuries, with higher incidence rates observed in cases resulting from high-energy trauma, such as motorcycle and car accidents, as well as in contact sports among athletes.[2] With increasing involvement of youth in sports activities there is increased incidence of these fractures. The other common mechanism of injury to posterior cruciate ligament is when force is applied to proximal tibia anteriorly when the knee is flexed. The functional impairment PCL injuries

can cause, may range from mild discomfort to severe functional impairment.[3] In cases having PCL avulsion fracture a history of posteriorly directed force on flexed knee or history of fall on flexed knee may be present. The physical examination may show presence of joint swelling, hemarthrosis or contusion over anterior tibia. Diagnosis may be confirmed on the basis of anteroposterior and lateral X-Ray of the affected knee which may show presence of bone discontinuity at the posterior tibial articular surface.[4] Computed tomography and MRI may help in further evaluation of fracture as well as identifying accompanying injuries such as meniscal tears or soft tissue involvement. Computed Tomography as well as MRI have a high sensitivity for the diagnosis of PCL avulsion fracture. PCL avulsion fractures usually involve tibial attachment and when this occurs it is essential to promptly diagnose and initiate appropriate management to optimize the clinical and functional outcome for patients.[5] Once diagnosed the treatment is usually surgical. Unlike in patients with isolated PCL injuries where the repair is usually deferred the cases with avulsion fracture needs prompt surgical intervention to prevent complications such as malunion and non-union. The repair can be done arthroscopically or by open reduction.[6] In developing countries arthroscopic surgeries are not commonly performed as arthroscopic surgeries are expensive and facilities as well as expertise to perform arthroscopic repair are not available except in urban areas. Therefor open reduction and internal fixation using screws remain one of the most commonly performed surgeries in rural and semi urban areas for PCL avulsion fractures. Various materials which can be used for internal fixation include lag screws, suture anchors, steel wires and straddle nails in addition to surgical management well designed rehabilitation program is also an essential part of management of these patients.[7] The clinical and functional outcomes of patients with PCL fractures treated by ORIF have been a subject of interest for researchers and clinicians alike. Understanding the long-term outcomes of open reduction and internal fixation for PCL avulsion fractures is crucial for guiding treatment decisions, optimizing surgical techniques, and improving patient care.[8] Numerous studies have investigated the efficacy of this surgical technique and its impact on patients' quality of life and functional recovery.[9] However many of these studies defined outcome on the basis of patients' subjective assessment of functional recovery

however in this study we used multiple objective scores to measure functional outcome. This was an observational study to analyze clinical and functional outcome of posterior cruciate ligament avulsion fractures from tibial attachment treated by open reduction and internal fixation.

Methods

The study was conducted in the Department of Orthopedics, Prakash Institute of Medical Sciences and Research Centre, Islampur, Sangli. India. The duration of study was 2 years from April 2021 to March 2023. In this study 40 adult patients of either gender with PCL avulsion fractures were included on the basis of a predefined inclusion and exclusion criteria. Using OPENEPI software version 3 on the basis of pilot study done on the PCL Avulsion fractures and assuming 90% power as well as 95% confidence interval sample size was determined to be enough if it was more than 35 patients thus 40 patients were included in this study. The inclusion criteria was adult patients with isolated PCL avulsion fracture diagnosed on the basis of imaging (X-Ray, Computerized Tomography and Magnetic resonance imaging) in whom PCL fragment was displaced more than 5 mm and those who presented within 4 weeks of injury. Patients who refused consent or those who presented after 4 weeks of injury and patients in whom PCL fragment was displaced less than 5 mm were excluded from the study. Patients with musculoskeletal conditions likely to affect the outcome assessment such as those having osteoarthritis, rheumatoid or psoriatic arthritis and those with multiple fractures were also excluded. A detailed history was taken from all the patients with respect to type of trauma and duration since injury. A through clinical examination was done by senior orthopedician in all the cases. Drawer test was performed to make a preliminary diagnosis of PCL injury. Imaging was done in the form of anteroposterior as well as lateral view radiographs of the affected knee. In selected cases 3D computed tomography (CT) was done. Since X-ray as well as CT has low sensitivity for assessment of soft tissue damage and injury to magnetic resonance imaging was done in selected cases. Preanesthetic evaluation was done in all the cases. Routine investigations such as complete hemogram, renal function tests, bleeding and clotting time and Hepatitis B and HIV ELISA was done in all the cases. In cases above 45

years of age physician's opinion regarding fitness for the surgery was also taken. All patients were treated by open reduction and internal fixation of avulsion fracture.

Surgical Procedure- The patient was given spinal anesthesia and placed in a prone position with the affected limb flexed. An inverted L-shaped incision was made, exposing the PCL tibial attachment through the interval between the medial gastrocnemius and semimembranosus, and the posterior knee capsule was incised to reveal the avulsed PCL tibial insertion fragment. The fracture hematoma was removed, and in cases of old injuries, any fibrous tissue was debrided from the avulsed fragment or its bed. Under C-arm guidance, the fractured fragment was visualized and repositioned over the posterior tibial plateau and sutured at the osteo-ligamentous junction. A long, thin guide wire was passed from the center of the fragment, directed from posterior to anterior through the proximal tibia, with the knee in flexion, ensuring it made a 45-degree angle to the posterior surface of the tibia. After safely drilling over the guide wire and measuring the length, a 4 mm cannulated cancellous screw with a washer was fixed in place. The fragment was reduced under direct vision to its bed (facilitated by slight knee flexion), gently held in place using a spike pusher, and provisionally fixed with a K-wire. The position of the reduced fragment was checked by fluoroscopy. Postoperative above knee slab given with padded support to superior part of calf to keep knee in anterior drawer position. Quadriceps exercises and non-weight bearing mobilization started from next day. Suture removal was done after 15 days. Passive knee bending started after 1 month with toe touch weight bearing. Full weight bearing started after full range of movements achieved after 6-8 weeks. Although full routine activities were allowed after 3 months, participation in contact sports was avoided till 9 – 12 months according to rehabilitation and muscle strength recovery. The patients were followed up every monthly till 3 months and after that every 3 months till 12 months. At every follow up visit patient clinical and functional assessment was done using Lysholm knee score (LKS) and Knee Society Score[10]. Qualitative data were represented in percentages and quantitative data was represented as mean with standard deviation. The statistical analysis was done using SSPS 22.0 software and p value less than 0.05 was taken as statistically significant.

Results

Fourty cases of posterior cruciate ligament avulsion fractures from tibial attachment treated by open reduction and internal fixation were included in this study of which there were 34 (75 %) were males and 6 (15%) were females with a M: F ratio of 1:0.17. 26 (65 %) of the participants had right side affected whereas remaining 14 (35 %) of the cases had left sided PCL avulsion fracture .The analysis of the age group of the patients showed that the most common affected age group was between 31-40 years (57.5%) followed by 41-50 years (27.50%). The mean age of affected patients was found to be 37.3 +/- 7.34 years (**T**able 1).

Out of 40 patients 29 (72.50%) patients sustained fracture secondary to road traffic accidents while 7 (17.50%) patients had sports related injuries. In 4 (10%) patients fracture was secondary to falls. Majority of the patients (52.50%) presented within 7 days of sustaining injury. 19 (47.50%) patients presented between 8 days to 4 weeks after injury (Table 2).

Functional assessment of the patients at the time of each follow up was done by Lysholm score as well as knee society score. At the time of presentation, the mean Lysholm score of the patients was found to be 4.5 +/- 2.8. There was gradual improvement in patients' Lysholm score with each follow up and at the time of 3 months the mean Lysholm score was found to be 72.8 +/- 9.2 whereas at the time of final follow up the mean Lysholm score was found to be 98.2 +/- 10.1. There was a significant improvement in Lysholm score from the time of presentation and at the time of final follow up and the difference was statistically highly significant (Fig. 1).

The functional assessment of the knee was also done by knee society score. At the

Table 1 Age Distribution of the Studied Cases

Age	No of cases	Percentage
18-30 years	3	7.50%
31-40 years	23	57.50%
41-50 years	11	27.50%
Above 50 years	3	7.50%
Total	40	100 %
Mean Age	37.3 +/- 7.34 years	

Table 2 Mechanism of Injury and Duration Since Injury

Mechanism and Duration of Injury		Number of Cases	Percentage
Mechanism of Injury	Road Traffic Accidents	29	72.50%
	Sports Injuries	7	17.50%
	Falls	4	10.00%
Duration Since Injury	Within 24 hours	9	22.50%
	2–7 days	12	30.00%
	8 days–2 weeks	10	25.00%
	15 days–4 weeks	9	22.50%

time of presentation, the mean knee society score was 34.16 +/- 12.34 which gradually improved to 82.76 +/- 10.36 at 6 months and at the time of final follow up the mean knee society score was 92.34 +/- 8.12. There was significant improvement in cases as assessed by knee society score (p<0.0001). At the time of presentation all patients were having moderate to severe pain. The mean VAS score at the time of presentation was 6.3 +/- 2.62. In postoperative period the pain reduced signifciantly over a period of weeks to months.

Table 3 Mean Knee Society Score at Presentation and During Follow Up

Comparison of Knee society and VAS scores		Mean +/- Std Deviation	P Value
Knee Society Score	At Presentation	26.34 +/- 9.98	P < 0.0001 (Paired t test) Highly significant
	At 1 Month	42.16 +/- 12.34	
	At 2 Months	46.78 +/- 14.62	
	At 3 Months	64.38 +/- 14.02	
	At 6 months	78.64 +/- 12.16	
	At 9 months	82.76 +/- 10.36	
	Final Follow Up (1 year)	88.20 +/- 8.12	
VAS Score	At Presentation	6.36 +/- 2.64	P < 0.0001 (Paired t test) Highly significant
	At 1 Month	3.94 +/- 1.84	
	At 2 Months	3.12 +/- 1.74	
	At 3 Months	2.68 +/- 1.36	
	At 6 months	2.12 +/- 1.22	
	At 9 months	1.80 +/- 0.92	
	Final Follow Up (1 year)	1.24 +/ 0.72	

Table 4 Outcome of Patients on the Basis of Knee Society Score

Outcome (KSS score)	Number of patients	Percentage
Excellent (80–100)	29	72.50%
Good (70–79)	6	15.00%
Fair (60–69)	4	10.00%
Poor (<60)	1	2.50%
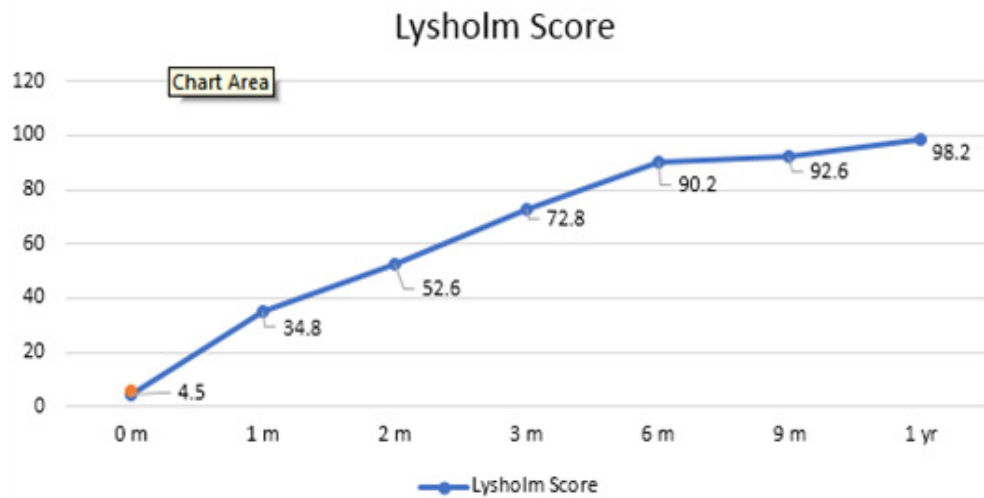
Fig. 1 Mean Lysholm Score at Presentation and During Follow Up

At the time of final follow up at 12 months there was significant reduction in VAS scores. At the time of final follow up the mean VAS score was found to be 1.24 +/- 0.72 (p<0.0001) (Table 3).

The final functional outcome as assessed by Knee society score showed that out of 40 cases 29 (72.50%) cases had an excellent outcome whereas 6 (15%) and 4 (10%) patients had fair outcome. Only 1 patient (2.50%) had KSS below 60 suggestive of poor outcome (Table 4).

The analysis of the patients on the basis of complications showed that out of 40 patients 32 (80%) patients didn't have any complications. 5 (12.5%) patients had residual intermittent pain, 2 (5%) patients had wound infections which was successfully treated by oral antibiotics and local wound care. Only 1 (2.5%) patient developed residual joint instability as evidenced by drawer test (Fig. 2).

Discussion

Posterior cruciate ligament injuries usually result from road traffic accidents or contact sports injuries. Unlike in cases of isolated PCL tears where the management remains controversial the guidelines for PCL avulsion fractures is unanimous and open reduction and internal fixation remains preferable line of management and conservative management
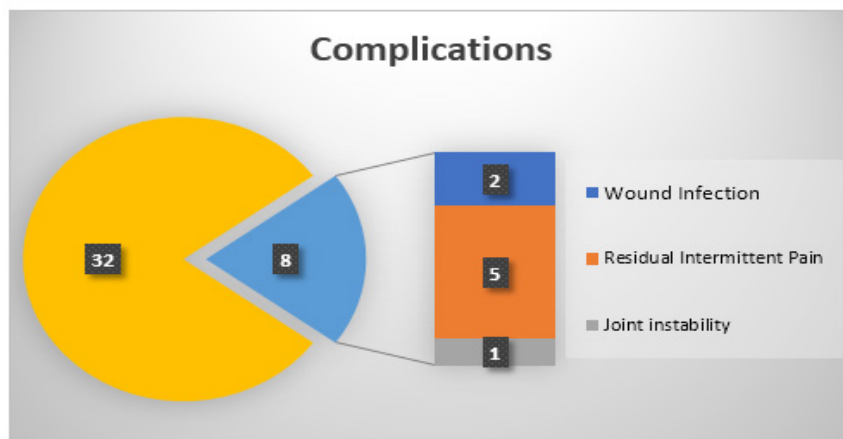
Fig. 2 Complications in the Studied Cases

is not desirable given the high chances of non-union or malunion which may further destabilize the affected knee.[11] In this study there was a significant male preponderance in cases of PCL avulsion fractures. Male preponderance is almost universal across the studies because of predominant involvement of males in road traffic accidents and contact sports which remains common causes of PCL avulsion fractures. Bali *et al.*[12] conducted a study to analyze the outcome of posterior cruciate ligament (PCL) avulsion fractures of tibia with open reduction and internal fixation.Forty-two patients (30 males and 12 females) with a median age of 26 years (range: 14–53 years) who underwent ORIF through a modified posterior approach for PCL fossa avulsion fractures were assessed after a median follow up of 18 months (range 10-42 months).In 30 patients' surgery was performed within 3 weeks of injury. This study showed a significant male preponderance with an M:F ratio being 1:0.4. Similar male preponderance was also reported by the authors such as Khatri *et al.*[13] and Fan *et al.*[14] The mean age of studied cases in this study was found to be 37.3 +/- 7.34 years. 29 (72.50%) patients sustained fracture secondary to road traffic accidents while 7 (17.50%) patients had sports related injuries. In 4 (10%) patients' fracture was secondary to falls. In western world most of the PCL injuries are result of what is popularly known as dashboard injuries where the injury occurs in sitting position and sudden abrupt force is applied on the anterior aspect of tibia. However, in developing world including in India PCL injuries are usually result of road traffic accidents involving bikes. Chen *et al.*[15] conducted a study to investigate the feasibility and clinical efficacy of using a toothed plate and hollow lag screw in the surgical treatment of posterior cruciate ligament (PCL) avulsion fractures of the tibia.This was a retrospective study of patients with PCL avulsion fractures of the tibia caused by road traffic accidents (n=9), sports-related injuries (n=6), falls (n=5) and machinery-related injuries (n=1). 20 patients presented with fresh fractures and one with an old fracture. The patients (13

men, eight women) had a mean age of 41.5 (range 19–72) years. The findings in this study were similar with respect to cause of avulsion fracture however the mean age of patients in this study was slightly higher. Similar findings were also reported by the authors such as Owesen *et al.*[16] and Sanders *et al.*[17] In this study all patients were treated by open reduction and internal fixation of avulsed part of tibia. Patients were followed up for 1 year. During follow up visits x-rays were taken to assess the union. Also, functional assessment was done using Lysholm score and knee society score. Both Lysholm and knee society score were found to gradually improve over the period of follow up and both there was a significant functional improvement in mean Lysholm and knee society score when compared from presentation to last follow up visit. In this study outcome assessment by KSS (Knee society score) showed that out of 40 cases 29 (72.50%) cases had an excellent outcome whereas 6 (15%) and 4 (10%) patients had fair outcome. Only 1 patient (2.50%) had KSS below 60 suggestive of poor outcome.

In a similar study Joshi *et al.*[18] performed open reduction and internal fixation using cannulated cancellous screws in 14 patients (mean age, 33.9 years) with isolated PCL avulsion injuries.At the time of final follow up the authors found The Lysholm functional score was excellent in 11 patients, good in 2 patients and fair in 1 patient with an average score of 97±7.6. Similar findings were also reported by the authors such as Wu *et al.*[19] and Khalifa *et al.*[20] Being a purely observational study, it has its inherent biases. A randomized control trial would be needed to further substantiate the outcome of this observational study. Moreover a prolonged follow up will be helpful in knowing long term complications of this treatment approach.

In conclusion, patients with posterior cruciate ligament avulsion fracture treated by Open reduction and internal fixation combined with quadriceps exercises in post-operative period were found to have excellent results in terms of functional outcome.

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Original Article

Conservative Management of Pott's Spine and Its Outcome: An Institute-Based Observational Study

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Abstract

Objective: To analyze the functional outcome of cases with Pott's disease treated solely by antitubercular drugs.

Methods: This observational study was conducted at the Department of Orthopedics of a tertiary care medical college. Sixty patients with Pott's disease were included in this study based on predefined inclusion and exclusion criteria. All patients received antitubercular drugs for nine months. The Modified McCormick Scale (MSS) was used to assess the outcome of patients.

Results: Out of 60 patients, 37 (61.67%) were females, and 23 (38.33%) were males, with an M: F ratio of 1:0.62. Most patients had some or the other risk factors and belonged to low socioeconomic status. The most common presenting complaint was low back pain, and the thoracolumbar spine was most commonly involved. There was a significant improvement in the patient's functional status as assessed by the MSS score.

Conclusion: If diagnosed early, patients with Pott's disease can be treated solely by antitubercular treatment with excellent outcomes.

Keywords: Functional outcome, mccormick scale, pott's disease, tuberculous spondylitis

Introduction

Pott's disease is the Mycobacterium tuberculosis infection of spine and is associated with significant morbidity and serious functional impairment. It is one of the most common forms of Tuberculous infection after pulmonary tuberculosis.[1] In most of the cases the initially the symptoms are non-specific therefor a high index of suspicion is necessary for an early diagnosis and prompt medical management of Pott's spine. A delay in diagnosis and antitubercular treatment is associated with catastrophic complications including paraparesis, scoliotic deformity and paraplegia. The tubercular infection reaches spine usually through hematogenous route and the common vertebral lesions include paradiscal, central and anterior sub ligamentous lesions.[2] Symptoms in initial stages of Pott's disease are non-specific and many a times these are attributed to less serious causes such as spondylosis. The common symptoms of Pott's disease include low grade fever, backache, unexplained weight loss and local tenderness. In many cases a past history of pulmonary tuberculosis may be present. In untreated cases neurological manifestations such as impaired sensations, radicular pain, paraparesis or paraplegia may be present. Unlike in other spinal pathologies neurological complications in cases of Pott's disease are usually symmetrical and gradually progressive. The clinical presentation may differ depending upon the site of involvement. The most common site affected in case of Pott's disease is thoracic spine followed by lumbar and cervical spine. If cervical spine is affected then it may lead to complications such as stridor, dysphagia and in serious cases paraplegia or even quadriplegia.[3] Once suspected the diagnosis of Pott's disease is usually confirmed on the basis of imaging techniques such as X-Ray,

computed tomography (CT) and magnetic resonance imaging (MRI). Though X-Ray of the spine is widely available however it has a very low sensitivity for the diagnosis of Pott's disease particularly in early stages because in early stages of disease the vertebral space is usually preserved. In some cases, X-Ray may show reduced vertebral height with the irregularity of endplate. In untreated cases the Pott's disease may present as gibbus deformity and vertebra plana. MRI is the imaging method of choice to assess the extent of involvement. MRI has a distinct advantage of showing presence of epidural component of the involvement as well as presence of cord compression. MRI may also show presence of paraspinal collection which may need surgical intervention.[4] The Pott's disease in majority of the cases managed by antitubercular drugs. Though the duration of treatment is a topic of debate majority of the researchers are of the opinion that the treatment should be continued for a total of 9 months. Total duration of treatment is divided into intensive phase (4 drugs given for 2 months) followed by continuation phase (2 drugs for 7 months). Surgical interventions are not needed if an early diagnosis is promptly followed by antitubercular treatment. In some cases, surgical procedures such as abscess drainage, laminectomy, costo-transversectomy or anterolateral decompression may be required. Novel techniques, such as minimally invasive spine surgery and implantable devices have also shown promising outcomes in selected cases.[5] This institution based observational study was undertaken to analyze the functional outcome of cases with Pott's disease who were treated only by antitubercular drugs.

Methods

This was an observational study conducted in the Department of Orthopaedics, Bharati Vidyapeeth Medical College and Hospital, Sangli, India. The study period was 2 years from April 2021 to March 2023. During this period 60 adult patients with Pott's disease who were treated solely by antitubercular drugs and having modified McCormick Scale (MSS) I, II or III at the time of presentation were included in this study. Patients having MSS IV or V at the time of presentation, those with pre-existing neurological diseases likely to affect the functional outcome and patients with congenital or acquired spinal deformities were excluded from the study. The sample size was calculated on the basis of pilot study done

on patients having Pott's disease, assuming 90% power and 95% confidence interval, the sample size required was 48 patients. Based on central limit theorem, sample size was determined to be enough if it was more than 50. Thus, 60 patients were included in this study. Demographic details such as age, gender and socioeconomic status were noted in all cases. A detailed history with respect to history of Kochs contact or any previous history of pulmonary or extrapulmonary tuberculosis was also asked and noted. Signs and symptoms such as presence of low-grade fever, backache or neurological symptoms and presence of sphincter involvement was enquired into. A thorough clinical examination was done with respect to presence of local tenderness or swelling over affected part of spine. A thorough general and neurological examination was done. Deep tendon reflexes were elicited and presence of any abnormality was noted. In all patients, routine investigations such as complete blood count, erythrocyte sedimentation rate (ESR), chest X-ray (to rule out presence of active or old pulmonary tuberculosis) was done in all cases. X-ray spine as well as Magnetic resonance imaging was also done in all cases. Percutaneous CT guided needle aspiration of abscess was done and the aspirate was sent for Acid fast bacillus (AFB) smear and culture sensitivity tests.

All patients received 2 months intensive phase of chemotherapy with four drugs (isoniazid (5 mg/kg, rifampicin 15 mg/kg, ethambutol 15–25 mg/kg), pyrazinamide (15–30 mg/kg) followed by 7 months of continuation phase comprising of 2 drugs (isoniazid and rifampicin). Patients were advised regular monthly follow up till 3 months and after that every 3 months till 15 months (last follow up visit was scheduled 6 months after completion of antitubercular treatment. During follow up visits routine investigations such as complete blood count, erythrocyte sedimentation rate (ESR), and detailed neurological examination was done. X-Ray of the affected spine was done every 2 monthly. In selected cases MRI was done during follow up visits if X-Ray was inconclusive. At the time of final follow up visit MRI was done in all the cases. During each follow up visit functional outcome was assessed using MMS which is used for assessment of global functional impairment in terms of neurological function and walking ability[6]. SPSS 21.0 software was used for data analysis. Descriptive statistics were depicted in the form of means and standard deviations for continuous variables, and frequencies

Table 1 Age Distribution and Socioeconomic Status of The Studied Cases

Demographic Profile		No of Cases	Percentage
Gender Distribution	Male	23	38.33%
	Female	37	61.67%
	Total	60	100 %
Age Group	18–30 years	7	11.67%
	31–40 years	21	35.00%
	41–50 years	17	28.33%
	Above 50 years	15	25.00%
	Total	60	100 %
	Mean Age	42.12 +/- 9.80 years	
Socio-Economic Status	Upper Class	1	1.67%
	Upper Middle Class	4	6.67%
	Middle class	15	25.00%
	Lower Middle Class	18	30.00%
	Lower Class	22	36.67%
	Total	60	100 %

and percentages for categorical variables. P value less than 0.05 was taken as statistically significant.

Results

Sixty patients diagnosed with Pott's disease and treated by antitubercular drugs for 9 months were included in this study. Out of 60 patients 37 (61.67%) were females and 23 (38.33%) were males with an M: F ratio of 1:0.62. The analysis of the age group of the patients showed that the most common affected age group was between 31-40 years (35 %) followed by 41-50 years (28.33 %). The mean age of affected patients was

Table 2 Predisposing Factors and Presenting Complaints of Studied Cases

Predisposing Factor and Presenting Complaints		No of Patients	Percentage
Predisposing Factors	H/o Pulm Kochs	13	21.67%
	H/O Kochs Contact	7	11.67%
	Hypertension	3	5.00%
	Diabetes	5	8.33%
	Hypertension and DM	2	3.33%
	HIV infection	7	11.67%
	Steroids/Immunosuppressant	3	5.00%
Presenting Complaints	Back pain	43	71.67%
	Low grade fever	34	56.67%
	Weight loss	23	38.33%
	Generalized weakness	13	21.67%
	Night sweats	5	8.33%
	Neurological manifestations	3	5.00%

**Table 3 MRI Imaging Features and Affected Site in Studied Cases**

	Age	No of cases	Percentage
MRI Imaging features	Vertebral body involvement	18	30.00%
	Disc Involvement	14	23.33%
	Endplate changes	12	20.00%
	Paravertebral Abscess	10	16.67%
	Gibbus deformity	6	10.00 %
	Total	60	100 %
Site of MRI changes	Thoracolumbar	32	53.33%
	Lumbar	16	26.67%
	thoracic	7	11.67%
	Lumbosacral	5	8.33%
	Total	60	100 %

found to be 42.12 +/- 9.80 years (Table 1). The distribution of the patients based on the Modified Kuppuswamy scale showed that in studied cases a majority of the patients belonged either to lower class (36.67%) or lower middle class (30 %). 15 (25%) patients belonged to middle class. Only 1(1.67%) patient belonged to upper class (Table 1).

The analysis of patients on the basis of predisposing factors or presence of co-morbidities showed that 13 (21.67%) patients had history of having received antitubercular treatment in past. History of recent contact with Kochs patient was found in 7 (11.67%) patients. 10 (16.67%) patients were having either diabetes mellitus or hypertension or a combination of both. 7 (11.67%) patients were HIV infected whereas 3 (5%) patients were on long term steroids or immunosuppressant. The analysis of patients on the basis of presenting complaints showed that the most common presenting complaint was low back pain which was seen in 43 (71.67%) patients. The other common complaints included low grade fever (56.67%), weight loss (38.33%) and weakness (21.67%). Night sweats and Neurological manifestations were seen in 5 (8.33%) and 3 (5.00%) patients respectively (Table 2).

On clinical Examination point of maximal
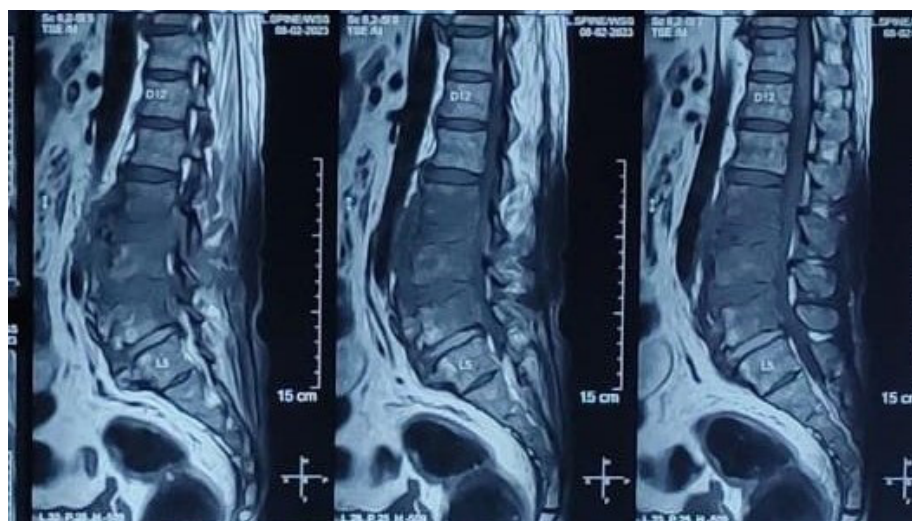
Fig. 1 Fusiform Pre- and Para-Vertebral Collections Seen Extending From L2 to L4 vertebrae. Affected Vertebrae Appears Hypo Intense on T1. Features s/o Tuberculous spondylitis

Table 4 Modified McCormick's Scale (MMS) in Studied Cases During Follow Up

Modified McCormick's scale (MMS)	1st Consultation	3 months	6 months	9 months	12 months		15 months	
I	29 (48.33%)	35 (58.33%)	58 (96.67 %)	58 (96.67%)	59	98.33 %	59	98.33 %
II	25 (41.67%)	23 (38.33%)	2 (3.33%)	2 (3.33%)	1	3.33 %	1	3.33 %
III	6 (10%)	2 (3.33%)	0 (0.00%)	0 (0.00%)	0	0%	0	0%
IV	0	0 (0.00%)	0 (0.00%)	0 (0.00%)	0	0 %	0	0 %
V	0	0 (0.00%)	0 (0.00%)	0 (0.00%)	0	0%	0	0%
Mean MMS	1.61 +/- 0.66	1.46 +/- 0.56	1.03 +/- 0.18	1.03 +/- 0.18	1.01 +/- 0.12		1.01 +/- 0.12	

tenderness was found in thoracolumbar region in 32 (53.33%) patients whereas lumbar, thoracic and lumbosacral area (8.33%) tenderness was found in 16 (26.67%), 7 (11.67%) and 5 (8.33%) patients respectively. All patients underwent MRI. The most common abnormality found on MRI was vertebral body involvement (seen as low signal on T1-weighted, high signal on T2-weighted images) which was seen in 18 (30.00%) patients followed by Disc Involvement (loss of disc height, altered signal intensity) which was seen in 14 (23.33%) patients. Endplate changes (20%), paravertebral abscess (16.66 %) and gibbus deformity (10%) were other MRI findings in studied cases (Table 3).

The functional assessment on the basis of MSS score showed that at the time of first consultation 29 (48.33%) patients belonged to MSS I whereas 25 (41.67%) and 6 (10%) patients belonged to scale II and III respectively. At the time of final follow up at 15 months 59 (98.33%) patients were found to have a MSS score of I (intact neurologically with no sensory or motor abnormalities) and 1 (1.67%) patient had MSS score of II (mild sensory deficit but functionally independent). There was remarkable improvement in functional status of the patient as assessed by MSS score and the difference was statistically highly significant (p<0.0001) (Table 4).

Discussion

In this study of patients having Pott's disease and treated solely by antitubercular management out of 60 patients 37 (61.67%) were females and 23 (38.33%) were males with an M:F ratio of 1:0.62. Jagiasi *et al.*[7] conducted a study of 44 patients diagnosed as Tuberculous spondylitis to delineate the importance of middle path regime and short course chemotherapy in the management of spine tuberculosis.[7] The analysis of gender distribution in this study showed that there was a significant male preponderance and out of 44 patients, 10 (22.73%) were males and 34 (77.27%) were females. Similar female preponderance was also reported by the authors such as Kothari[8] and Peer *et al.*[9] The mean age of patients in this study was found to be 42.12 +/- 9.80 years. Wang *et al.*[10] conducted a study of 44 patients with Pott's disease.For this purpose the authors collected data of 597 patients with Pott's disease. These patients had no major neurological deficits or severe spinal deformities. The study population consisted of 313 male (52.43 %) and 284 female (47.57 %) patients, with a mean age of 43 years (range 13–89 years). The mean age of patients in this study was found to be similar to this study. Similar mean age of patients with Pott's spine was also reported by the authors such as Divya *et al.*[11] and Mittal *et al.*[12]. The analysis of patients on the basis of predisposing factors or presence of co-morbidities showed that 13 (21.67%) patients had history of having received antitubercular treatment in past. History of recent contact with Kochs patient was found in 7 (11.67%) patients. Other predisposing factors in this study were immunosuppression due to HIV and long-term steroid therapy. Previous history of pulmonary tuberculosis and immunocompromised status were common factors leading to Pott's disease in many of the studies. Vaishnav B *et al* conducted an observational study of 100 cases of Pott's spine.[13] These findings were similar to the findings of this study since in this study also majority of the patients had either previous history of pulmonary tuberculosis. Similar predisposing factors were also reported by the authors such as Jurcev-Savicevic *et al.*[14] In this study majority

of patient's belonged lower and lower middle class and poor socioeconomic status was a significant factor seen in patients presenting with Pott's disease. Glassman *et al.*[15] also reported malnutrition and poverty to be one of the significant risk factors for development of Pott's disease.In this study most common area involved was thoracolumbar area. MRI showed involvement of either thoracic or lumbar or thoracolumbar vertebrae in majority of the cases (91.67%) cases. Only in 5 (8.33%) patients' lumbosacral area was involved. The most common abnormality found on MRI was vertebral body involvement (seen as low signal on T1-weighted, high signal on T2-weighted images) (30.00%) followed by Disc (23.33%) patients. Endplate changes (20%), paravertebral Abscess (16.66 %) and gibbus deformity (10%). Misra *et al.*[16] conducted a study of MRI findings in patients of Pott's disease. For this purpose the author's analyzed MRI findings of 36 patients with Pott's disease. The authors found vertebral changes in form of spondylodiscitis in 33 (92%), epidural abscess in 29 (81%), spinal cord changes including edema and granuloma in 17 (47%), paravertebral abscess in 29 (81%), and vertebral body collapse in 12 (33.3%) patients. Similar MRI findings in cases of Pott's disease was also reported by the authors such as Rivas-Garcia *et al.*[17] and Kubihal *et al.*[18] All the patients were treated by antitubercular

treatment for 9 months and were followed up till 6 months after completion of antitubercular treatment. Patients' functional outcome was assessed by MMS. There was a significant improvement in functional status of the patient as assessed by MSS score and the difference was statistically highly significant (p<0.0001). No patient had any significant impact on functional independence and only 1 patient had mild sensory disturbance at the time for final follow up. Similar excellent outcome after complete course of antitubercular treatment was also reported by the authors such as Talebzadeh *et al.*[19] and Bakhsh *et al.*[20] Pott's disease or tubercular spondylitis needs early diagnosis and prompt antitubercular treatment for adequate period of time. Patients diagnosed early can be successfully treated by antitubercular drugs without any need for surgical interventions. Majority of the adequately treated patients have excellent functional outcome without any residual motor or sensory disturbance.

The main limitation of this study was that it was a purely observational study. More randomized controlled trials are needed to further substantiate findings of this study.

In conclusion patients with Pott's disease if diagnosed early can be treated solely by antitubercular treatment and have excellent outcome and remain intact neurologically with no sensory or motor abnormalities.

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Rahil Jiwani, Sourabh Ghosh, *et al*

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Association between Comorbidities and COVID-19 Mortality: a Cross-Sectional Study in a Community Health Center in Indonesia

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Abstract

Objective: To analyze the risk factors for mortality and comorbidity of COVID-19 patients in a public health center work area in Indonesia.

Methods: This was a cross-sectional observational analytic quantitative study using secondary data of 820 confirmed COVID-19 cases in Brebes Public Health Center work area during the period of June 2020–December 2021. Univariate and bivariate analyses were used to analyze the obtained data statistically with a p-value of <0.005 considered significant.

Results: Of the 820 confirmed COVID-19 patients, 85.1% recovered and 15.0% died. Analysis on the characteristics of these cases showed that 51.2% females and 48.8 % males were included in this study, with 77.6% of them were <60 years old. No history of comorbidities was identified in 92.1% of the cases. In remaining cases with comorbidities, Diabetes Mellitus was recognized as the most prevalent (n=39, 4.8%). Results of the Chi-Square test demonstrated that comorbidity status (p-value= 0.001), place of quarantine (p=0.000; p>0.05), and diabetes (p=0.000, OR =2.87, 95% CI 19 1.24–0280) were significantly associated with mortality.

Conclusion: Comorbidity status, diabetes, and the place quarantine are risk factors for mortality among COVID-19 confirmed cases, especially in Brebes Public Health Center work area. Thus, it is important to increase knowledge about COVID-19 prevention and risks to prevent transmission among those with higher risks for mortality. Further studies on factors related to sustainable supports for COVID-19 patients are also necessary.

Keywords: Characteristics, comorbidity, COVID-19, risk factors

Introduction

Amount COVID-19 cases continue to increase, progress very quickly, and spread around the world. The etiology of COVID-19 is *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2). The exposure process or SARS-CoV-2 transmission is from man to man to another, with characteristics of potential aerosol transmission. Transmission becomes easier on the environment closed because it makes the virus concentrate for persisting for a long time Li *et al*. With characteristics such as a contagion easy, then the COVID-19 pandemic still Keeps going and continues and amounts increasing cases.[1] Until On 15 December 2021, WHO reported 318,648,834 cases confirmation with 518,343 deaths worldwide (CFR 1.7%). Indonesia there are 4,270,794 cases confirmed , 4,118,164 Cases Cured (96.4%), 7,877 Cases Active (0.2%) and 144,167 Cases died (CFR 3.4%).[2] province with case biggest is DKI Jakarta Patient Positive 870,363, Recovered 852,973, Died 13,611, West Java Patient Positive 709,515, recovered 693,895 died 14,761, Central Java Patient Positive 487,098, recovered 455,763 (RR 93.56%), died 30,297 (CFR 6.2%) Central Java occupies order first based on cumulative case COVID-19 deaths.[3] In Brebes Regency until On December 15, 2021 there were 14,177 cases confirmed, 12,405 recovered

completely, died 1,607 (CFR 8.8%). 5 Health Centers with case highest is Brebes Health Center Patients confirmed 1775, died 244, Puskesmas Bumiayu Patient confirmed 1587, died 127, Puskesmas Banjarharjo Patient confirmed 1095, Patient died 100, Puskesmas Bulakamba Patient confirmed 1108, Patient died 177, Puskesmas Liability Patient confirmed 850, Patient died 99.[4] Results of studies conducted obtained a vulnerable group infected with COVID-19, including carry-on group age (elderly), disease attendant, smoker vape smokers, men, and individuals with group blood A. Besides SARS, CoV-2 infection also more easily happens to someone who experiences drop system immune. In addition, individuals who have other diseases will find more easily more exposed to viral infection.[5] Signs and symptoms of general COVID-19 infection in the form of symptom disturbance respiration I like fever, cough, and shortness of breath. COVID-19 case degrees heavy could cause pneumonia, respiratory failure, kidney disease, and even death.[6,7] Based on Dessie & Zemotir's research, several risk factors influence death due to the coronavirus, namely chronic comorbidity, complications, and demographic variables including acute kidney injury, COPD, diabetes, hypertension, CVD, cancer, increased D-dimer, male gender, age older, active smoker, and obese.[8]

This study aimed to summarize available findings on the association between comorbidities, complications, smoking status, obesity, gender, age and D-dimer, and risk of mortality from COVID-19 using a large dataset from a number of studies. Method: Electronic databases including Google Scholar, Cochrane Library, Web of Sciences (WOS Apart from that, research by Djaharuddin *et al.*,[9] stated that the most deaths due to comorbidities were hypertension, cardiovascular disease, and diabetes. More than half of the patients (52.56%) who died due to COVID-19 had ≥2 comorbidities and the rest had only one comorbidity.[9] By looking at COVID-19 cases in Brebes Regency and the risk factors that influence them, this study aimed to analyze the relationship between risk factors for case fatality and comorbidities.

Methods

This is a quantitative study with a design observational analytic with the cross-sectional approach. Data collection was carried out after obtaining permission according to No. 055/0243/I/2022 from the Brebes Public Health Center. Data used is secondary data at the Brebes Public Health Center for the period June 2020–December 2021, with the amount case at most 820 confirmed data for covid and death covering age, gender, comorbidities, history treated, and symptoms. A number of Research samples is the total population, namely 820 respondents. The data was obtained from the report documents of confirmed COVID-19 patients at the Brebes Community Health Center. There are inclusion criteria, namely all patients diagnosed with COVID-19 at the Brebes Health Center for the period June 2020 - December 2021. Exclusion criteria, namely incomplete medical records of the required variables. Scoring criteria based on gender and age: cured (1), Die (2); male (1), female (2); >60 years (Cont. age) (1) 45 – 59 years (Pra carry on age); 19 – 44 years (Adult) (2); 10–18 years (Teenagers); 6 – 9 years (Child) (3), 1–5 years (Toddler) (4); 0 years (Baby) (5). Scoring criteria based on comorbidities: Comorbidity Status, Diabetes Mellitus, Hypertension, Pneumonia/ARI, Fail Heart, Rheumatoid Arthritis, and Asthma with the answer being Yes (1); No (2). Statistical test is used to calculate the p-value of each Chi-square test variable used in the analysis process. Microsoft Excel and SPSS v.24 were used to perform univariate and bivariate (Chi-square test) analysis.

Table 1 Distribution Characteristics Patient Confirmed COVID-19 by Gender and Age (n=820)

Variable	n=820	%
Patient Status		
Cured	698	85.0
Die	122	15.0
Gender		
Male	400	48.8
Female	420	51.2
Age		
>60 years (Cont. age)	183	22.5
45–59 years (Pra carry on age)	261	31.8
19–44 years (Adult)	321	39.3
10–18 years (Teenagers)	25	3.1
6–9 years (Child)	11	1.3
1–5 years (Toddler)	14	1.7
0 years (Baby)	5	6

Results

The following is the characteristics of respondents COVID-19 patients based on confirmed status, gender, and age. Table 1 describes out of the 820 confirmed COVID-19 patients, 85.1% were declared recovered, and as many as 15.0% were declared dead. Based on type sex, as many as 51.2% are females and as many as 48.8 % males. Most age suffering from COVID-19 is <60 years old, that is as much as 77.6%.

Based on Table 2 shows that of 820 patients who did not have a history of comorbidity, as many as 92.1% and who had comorbidity status as much as 7.9%. The most identified comorbidity was diabetes Mellitus in as many as 39 people (4.8%).

Based on Table 3 it is known that out of 820 patients who had a history of hospitalization, as many as 548 (66.8 %) and a history of

Table 2 Characteristic Distribution Patient Confirmed COVID-19 based on Comorbidities

Variable	n=820	%
Comorbidity Status		
Yes	65	7.9
Not	755	92.1
Diabetes Mellitus		
Yes	39	4.8
Not	781	95.2
Hypertension		
Yes	20	2.4
Not	800	97.6
Pneumonia/ARI		
Yes	9	1.1
Not	811	98.9
Fail Heart		
Yes	3	0.4
Not	817	99.6
Rheumatoid Arthritis		
Yes	1	0.1
Not	819	99.9
Asthma		
Yes	1	0.1
Not	819	99.9

Table 3 Characteristic Distribution Patient Confirmed COVID-19 based on The place Quarantine

The place Quarantine	n=820	%
Isolation Independently	272	33.2
Hospital	548	66.8
RS Umum Pusat Kariadi	6	0.7
RS Umum Daerah Brebes	299	36.5
RS Umum Bhakti Asih	109	13.3
RS umum Islam Harapan Anda	58	7.1
RS umum Mitra Keluarga	17	2.1
Puskesmas/Isolasi Mandiri	272	33.2
RS Umum Hermina Panandaran	2	0.2
RS Umum Daerah Kardinah	20	2.4
RSUD Soseselo slawi Kab Tegal	11	1.3
RSU Islam mutiara Bunda	3	0.4
RS Mitra Siaga Tegal	4	0.5
RS Bhakti Asih Kec. Jatibarang	6	0.7
RSUD Dedy Jaya Brebes	11	1.3
RSUD Surodadi Tegal	1	0.1
RS Harapan Sehat Bumiayu	1	0.1

isolation independent as 272 people (33.2 %). Most treated patients at the Brebes Hospital as many as 299 people (36.5%).

Based on Chi-Square test results, related variables with the case confirmed COVID-19 is comorbidity status shows p-value=0.001 where the p-value is less than <0.05, then by statistics showing there is a connection between comorbidity status with the case confirmed COVID-19 at the Brebes Health Center with OR 0.383, 95% CI (19) 0.216–0.680 it means the age of morbidity status have opportunity risky 0.383 times cause confirmed COVID-19 (Table 4). Diabetes variable with p=0.000 <0.05 means that there is a significant relationship between diabetes status and cases confirmed COVID-19 with OR value 2.87 with 95% CI 19 1.24-0280 mean people who have a history of diabetes have an opportunity risky 2.87 times cause death due to COVID-19 compared with people who don't have a history of diabetes (Table 4).
Based on the Chi-Square test results variable, the place quarantine shows a score *of p*=0.000

Table 4 Correlation of Death Status and Comorbidities

Variable	Status				p	OR	95% CI	
	Cured		Die				Lower	Upper
	n	%	n	%				
Comorbidity						0.383	0.216	0.679
Yes	46	6.6	19	15.7	0.001			
Not	652	93.4	103	84.3				
Diabetes						2.87	0.144	0.569
Yes	25	3.6	14	11.5	0. 000			
Not	673	96.4	108	88.5				
Hypertension						0.514	0.183	1.441
Yes	15	2.1	5	4.1	0.198			
Not	683	97.9	117	95.9				
ARI						0.608	0.125	2.961
Yes	7	1	2	1.6	0.534			
Not	691	99	120	98.4				
Fail Heart						1.176	1.142	1.210
Yes	3	0.4	0	0	0.468			
Not	695	99.6	122	100				
RD Arthritis						1.175	1.142	1.209
Yes	1	0.1	0	0	0.676			
Not	697	99.9	122	100				
Asthma						1.175	1.142	1.209
Yes	1	0.1	0	0	0.676			
Not	697	99.9	122	100				

>0.05, which means that there is a significant relationship between place quarantine with the case confirmed COVID-19. Place Variable Quarantine shows a significant relationship between places quarantine with the death confirmed COVID-19 cases with *p*=0.000 >0.05 (Table 5).

Discussion

Variable comorbidity status shows there is an association between comorbidity statuses with the death case at the Brebes Health Center. This research result is in line with research in Ternate City, North Maluku, which reports that disease comorbidity like hypertension, diabetes mellitus type 2,

Table 5 Relationship of The place Quarantine with Death Case of COVID-19

Variable	Status				p		95% CI	
	Cured		Die			OR	Lower	Upper
	n	%	n	%				
The place Quarantine						0.777	0.743	0.813
Hospital	426	61	122	100	0.00			
Isolation Independent	272	39	0	0				

and asthma have a significant relationship (p≤0.05) to the severity of COVID-19 disease.[6] A meta-analysis study shows that the existence of comorbidities in COVID-19 patients increases the severity of the disease by around tripled (OR=2.85, 95%IK=2.09-3.89).[7] Mechanism-related pathophysiology with risk more severity high in COVID-19 patients with comorbidity is condition chronic that causes dysregulation system physiological main, including axis hypothalamus - pituitary -adrenal, system nerve sympathetic, and immune systems.[8] The COVID-19 virus can also induce or make it worse condition with tie receptors *Angiotensin-Converting Enzyme* 2 (ACE2) which is spread in various organs so that disturb the function of the renin-angiotensin-aldosterone system (RAAS), causes disturbance hemostatic, nervous, and systemic physiological main so that more easy experience more organ failure more to come to increase COVID-19 complications and deaths.[9] This study finds that type of disease associated with comorbidities by a significant degree of clinical COVID-19 is diabetes, where diabetes shows a significant relationship between Diabetes status and cases confirmed COVID-19 with p=0.000 <0.05. This is in line with research by Lee, that patients with diabetes mellitus type 2 can increase the severity of COVID-19 patients by 1.55 times compared with COVID-19 patients who do not suffer from diabetes mellitus.[10] People with diabetes mellitus with COVID-19 will increase hyperglycemic hormone secretion like catecholamines and glucocorticoids, producing elevation glucose in blood variability, abnormal glucose, and diabetes complications.[11] Diabetes is one of the factors risk main COVID-19 occurs. This thing because more diabetics are susceptible to infection because of conditions hyperglycemia, disorders of function immunity, complications vascular and disease attendants like hypertension, dyslipidemia, and cardiovascular disease. Severity and mortality from COVID-19 directly mean higher in patients with diabetes than non-diabetic patients.[12]

People with diabetes mellitus with COVID-19 will increase secretion hormone hyperglycemic like *catecholamines* and *glucocorticoids* with produce elevation glucose in the blood, abnormal variability glucose, and diabetes complications.[12] Two Another study conducted in Indonesia found that the results are in line with where diabetes mellitus is a factor of comorbidities that can increase the severity of COVID- 19 disease by 3.4 times as well as

increase the risk of 4.4 times more deaths more big compared to patients without comorbid diabetes mellitus.[13,10] Variable hypertension showed no significant relationship between comorbid hypertension and cases confirmed COVID-19 with p=0.119 >0.05. The same research was also conducted in 2020 with the results of the study with a Chi-Square statistical test that p-value=0.414 (p>0.05), so could conclude that no there is a significant relationship between sufferer hypertension and with condition COVID-19 incident.[17]

Study this no inline study According to Li[18] stated as many as 17.1% of patients with a history of infectious diseases, one of which is hypertension, so that hypertension is a comorbid infectious disease, one of which is COVID-19 among 1,527 patients who are spread out to be treated in ICU and non-ICU.Some studies show the disease of comorbid hypertension could worsen the prognosis of COVID-19 because consumption of ACE inhibitors and ARBs as intervention drug hypertension, it turns out, could exacerbate COVID-19.[18] Based on theory, the underlying mechanism connection Between hypertension and COVID-19 is still not yet known. However, considering the role important RAS (Renin Angiotensin System)/ACE-2 in the pathophysiology of hypertension, dysregulation from the system is a possible role important. Based on the thing, it has also submitted something draft that therapy hypertension with SRA inhibitors can affect the binding process of SARS-CoV-2 to ACE-2, supporting the infection process. Suggestion based on experimental findings that RAS inhibitors that cause enhancement ACE-2 expression as compensation from therapy and ACE blockers can character detrimental in patients exposed to SARS-CoV-2.[19] Variable hypertension showed no significant relationship between ARI comorbidities and cases confirmed COVID-19, COVID-19 with p=0.535 >0.05. This thing is in line with research Komang, which shows no connection characteristics between ARI visitors with the incidence of COVID-19 (p>0.05). Characteristics that coverage, employment status, and gender.[20] Study this in line with merlin research factor risk comorbid to the incidence of COVID-19 at the City Health Center in 2020 is concluded that results analysis bivariate state that Pneumonia is not had significant relationship to the incidence of COVID-19 at the City Health Center in 2020.[6]

In severe cases, COVID-19 can exacerbate with acute respiratory distress syndrome,

sepsis, septic shock, and multi organ failure, including failed kidney or heart failure. [21] Variable hypertension showed no significant relationship between comorbid Fail Heart with the case confirmed COVID-19 with p=0.468 >0.05. This is similar to previous research by Steven, which states there was no significant relationship between history disease heart with vulnerability suffering from COVID-19 compared to with Pneumonia non-COVID-19 seen based on statistical test results chi-square obtained p value =0.828 (p>0.05).[19] In contrast with Zheng research, patients with comorbid cardio-vascular hypertension and heart coronary disease (CHD) are riskier of experiencing manifestation heavier if infected with SARS-CoV-2 and contributed to part significant case death in COVID-19. This is probably because more ACE2 expression is high in patients with cardiovascular disease.[18] Patients >60 years old infected with SARS-CoV-2 can experience more systemic and critical pneumonia manifestations compared to patients 60 years of age and aggravated by comorbid cardiovascular disease.[22] Patients with a history of cardiovascular disease could become unstable in a state infected with SARS-CoV-2 due to imbalance. Among needs increased metabolism because of infection and decreased backup heart. Patients with syndrome coroner Acute infections (ACS) infected with SARS-CoV-2 often have poor prognoses. In ACS patients, reserved functional heart reduces the ischemia or necrosis myocardium, so when infected with SARS-CoV-2, insufficiency heart could happen, cause bad suddenly. Some COVID-19 patients in Wuhan have a history of ACS, related to the more severe disease, and have a high mortality rate.[20,21] Research results different with study can because sufferer disease heart from a sample taken Only a little consume drug hypertension ACEIs or ARBs that can increase possibility suffering from COVID-19 routine. Variable asthma showed no significant relationship between comorbid asthma with the case confirmed COVID-19 with p=0.676 >0.05. Coronavirus is a virus that attacks system breathing. The coronavirus is the same as a respiratory virus; others could make symptoms experienced asthma increase bad as well as possible experience an attack threatening asthma life. The World Health Organization also lists the diseases asthma, diabetes, and heart disease as conditions that make somebody more susceptible becomes sick due to coronavirus. Coronavirus infection attacks respiration in the lungs and then damages the heart. People with cardiovascular disease and hypertension risk more of getting infected and experiencing fatality due to the coronavirus. Coronavirus infection looks more critical than other viruses because it can cause damage to the heart muscle and heart injuries like pericarditis and myocarditis. According to the study by Winogroho,[23] the place quarantine has a significant influence on the healing process and shortens the quarantine period for exposed nurses to COVID-19. This study shows that the place quarantine contributes positively to the length of time quarantine. The individual will feel comfortable if they are in an environment that is comfortable and supportive for the healing process. This is in line with a study by Wang stated that infection nosocomial is hazardous for the sufferer or other patients treated as well as healthy people.[24] At Zhongnan Hospital reported, the first patient only symptom sick stomach. Then he was treated at the same hospital with COVID-19 patients and finally infected COVID-19 patients. Besides that, more than ten hospital workers were infected with this disease. This thing no in line with the study reveals several factors risks determined by the Centers for Disease Control and Prevention (CDC): contact closely, including stay one house with COVID-19 patients, and historical journey to the affected area. In one environment, however, no contact close (within a radius of 2 meters) is considered risk low.[26] Currently, the spread of SARS-CoV-2 from man to man has become the source transmission main, so deployment becomes aggressive. Transmission of SARS-CoV-2 from patient symptomatic occurs through the *droplet* that comes out moment cough or sneezes. [22,27] Spread of the virus from man to man occurs because to do contact close with an infected person; coughing, sneezing, or aerosol. This aerosol could penetrate the body, especially the lungs, through inhalation through the nose or mouth. Coronavirus also shows level transmission taller than SARS because recombination genetics have increased ability transmission Shereen.[28]

In this study, only COVID-19 cases occurred at the Brebes Community Health Center. For this reason, further comprehensive research is needed to determine the risk factors that influence COVID-19 comorbidity and mortality.

The conclusion is risk factors that have a significant association on the death confirmed COVID-19 case in the work area Brebes Community Health Center, namely

the status of comorbidity, diabetes, and the place quarantine. The factor that most influences comorbidities on COVID-19 deaths is diabetes mellitus. The recommendation for the Public is to increase knowledge about Covid 19 prevention and the need to study sustainability for support related factors with the case confirmed COVID-19.

Acknowledgements

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Original Article

Comparison of Coagulation Parameters between Severe and Non-severe COVID-19 Patients Treated in a Tertiary Hospital in Indonesia

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Abstract

Objective: To determine the differences in coagulation features in patients with severe versus non-severe COVID-19.

Method: During the period of the study from July 2020 to June 2021, 371 COVID-19 patients were treated at Dr. Hasan Sadikin General Hospital Bandung, Indonesia. These patients were divided into two groups based on the WHO criteria into severe COVID-19 with clinical signs such as severe acute respiratory syndrome to respiratory failure and non-severe cases with no respiratory symptoms. Data analyzed were Prothrombin Time (PT), Activated Partial Thromboplastin Time (aPTT), International Normalized Ratio (INR), fibrinogen, D-dimer, and platelet count.

Results: Median INR was significantly higher in patients with severe cases than in non-severe cases (1.04 vs. 0.94, p<0.001), which was also true for median PT (12.3 vs. 12.0 sec, p=0.030) and median fibrinogen (522 vs. 428.5 mg/dL, p=0.004). Similarly, the median D-dimer was significantly higher in severe patients (1.91 vs. 0.75 mg/dL, p<0.001). Median aPTT and platelet count were in normal limits for both severe and non-severe COVID-19 patients (28.6 vs. 29.15 sec, p>0.652 and 246 vs. 242 x10^3/mm^3, p>0.924, respectively).

Conclusions: The INR, PT, fibrinogen, and D-dimer can be considered as features that can be used to predict the severity of the disease and to choose the proper treatment for COVID-19 patients.

Keywords: Coagulopathy disorders, COVID-19, severe acute respiratory syndrome, non-severe acute respiratory syndrome

Introduction

The status of Coronavirus Disease 2019 (COVID-19) is still designated a global pandemic by WHO. The current case of COVID-19 is still a global problem, including in Indonesia, with severe complications and even death. Several previous studies have found that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a receptor at the cellular level to facilitate the infection process and is widely expressed in various human body tissues such as the lungs, gastrointestinal tract, heart, kidneys, and endothelium of blood vessels. These tissues serve as entry points for SARS-CoV-2 infection and replication through a direct cytopathic effect.[1-3] The clinical manifestations of COVID-19 patients have a broad spectrum from mild to severe symptoms such as Acute Respiratory Distress Syndrome (ARDS), multiple organ failure, COVID-19 Associated Coagulopathy (CAC), and death. COVID-19 Associated Coagulopathy (CAC) is associated with disease morbidity and mortality. The most

common manifestations of CAC are venous thromboembolism (VTE), such as deep vein thrombosis (DVT) or pulmonary embolism (PE). The high incidence of VTE in COVID-19 patients reveals the importance of coagulation parameter examinations to make a diagnosis and treat the patient.[4-8] The coagulation parameter is a quantitative parameter to assess the progression of COVID-19. Coagulation parameters are D-dimer, prothrombin time (PT), Activated partial thromboplastin time (APTT), International Normalized Number (INR), fibrinogen, and platelet count.[8, 9] Clinicians can diagnose accurately and quickly in managing COVID-19 patients if they understand the differences in coagulation parameters between severe and non-severe COVID-19. This study was conducted to determine the differences in coagulation parameters between severe and non-severe COVID-19 patients at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia.

Methods

This study was an analytical descriptive retrospective of the medical records of COVID-19 patients conducted in Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. The subject consist of 317 COVID-19 patients, divided into two groups, severe and non-severe COVID-19, from June 2020 to July 2021. Inclusion criteria subject consist of age over 18 years with severe and non-severe COVID-19 patients. The clinical signs of severe patient such as severe acute respiratory syndrome to respiratory failure and non-severe patients which is no respiratory symptom COVID-19 according to WHO criteria. Exclusion criteria are patient was treated anticoagulant before and have any disease such as hemostasis disorders, autoimmune, neoplasm, and pregnancy. The data were analyzed using the Mann-Whitney test. This study has been approved by the Health Research Ethics Committee Dr. Hasan Sadikin General Hospital Bandung, No. LB.02.01/X.6.5/323/2021.

Results

Subject who met the inclusion and exclusion criteria, divided into 99 severe COVID-19

Table 1 Subject Characteristics

Variable	Groups		p-value
	Severe COVID-19 n=99	**Non-severe COVID-19 n=218**	
Age (years old), median (min-max)	57 (29–89)	52 (19–88)	<0.001[a]*
Gender, n (%)			
Female	43 (43.4)	109 (50.0)	0.278[b]
Male	56 (56.6)	109 (50.0)	
Comorbid, n (%)			
Yes	75 (75.8)	112 (51.4)	<0.001[b]*
No	24 (24.2)	106 (48.6)	
Type of Comorbid, n (%)			
Hypertension	45 (45.5)	61 (28.0)	0.002[b]*
Diabetes Mellitus	26 (26.3)	34 (15.6)	0.025[b]*
Cardiovascular Disease	17 (17.2)	14 (6.4)	0.003[b]*
Chronic Kidney Disease	6 (6.1)	6 (2.8)	0.202[c]
Chronic Pulmonary Disease	4 (4.0)	4 (1.8)	0.263[c]
Neurological Disease	3 (3.0)	3 (1.4)	0.381[c]
Liver Disease	2 (2.0)	1 (0.5)	0.231[c]
Rheumatic Disease	1 (1.0)	1 (0.5)	0.528[c]
HIV/AIDS	0 (0.0)	1 (0.5)	1.000[c]

[a]Mann Whitney test, [b]Chi Square test, [c]Fisher Exact test, * p<0.05

Table 2 Coagulation Parameters and the Clinical Outcomes

Variable	Groups		P value
	Severe COVID-19 n=99	**Non-severe COVID-19 n=218**	
Laboratory, median (min-max)			
Days of illness (th days)	8 (5–10)	6 (3–9)	0.001[a]*
INR	1.04 (0.93–1.14)	0.94 (0.89 –1.00)	<0.001[a]*
PT (seconds)	12.3 (11.0–14.2)	12.0 (10.5–13.6)	0.030[a]*
aPTT (seconds)	28.6 (24.3–34.7)	29.15 (24.8–33.0)	0.652[a]
Fibrinogen (mg/dL)	522 (350–680)	428.5 (329–564)	0.004[a]*
D-Dimer (mg/dL)	1.91 (0.80–9.57)	0.75 (0.40–1.82)	<0.001[a]*
Platelet (x10^3/mm^3)	246 (172–309)	242 (179–307)	0.924[a]
Outcome, n (%)			
Survival	62 (62.6)	203 (93.1)	<0.001[b]*
Death	37 (37.4)	15 (6.9)	

Median (IQR), [a]uji Mann Whitney, [b]uji Chi-Square, * p<0.05

patients and 218 non-severe patients. The primary characteristics of the patients are shown in Table 1.

Table 1 revealed that age, comorbidities, comorbid types of hypertension, diabetes mellitus, and cardiovascular disease between the two groups had significant differences (p<0.05). The median age of severe COVID-19 patients was 57 (range: 29–89 years old), while non-severe COVID-19 patients were 52 (range: 19–88 years old). Severe COVID-19 patients had more comorbidities than non-severe COVID-19 (75.8% vs. 51.4%, p<0.001). Severe COVID-19 comorbidities were 45.5% hypertension, 26.3% diabetes mellitus, and 17.2% cardiovascular disease, while non-severe COVID-19 had 28.0% hypertension, 15.6% diabetes mellitus, and 6.4% cardiovascular disease.

Table 2 revealed significant differences in days of illness, INR, PT, Fibrinogen, D-Dimer, and patient outcomes between the two groups (p<0.05). The median illness day of the severe COVID-19 group was higher than the non-severe COVID-19 group (p=0.001). The median INR and PT of the severe COVID-19 group were higher than the non-severe COVID-19 group with significantly (p<0.001) and (p=0.030), respectively. The severe COVID-19 group had median fibrinogen and D-dimer higher than the non-severe COVID-19 group (p=0.004) and (p<0.001) respectively. The mortality percentage of the severe COVID-19 group was higher than the non-severe COVID-19 group (p<0.001).

Discussion

The number of new cases of COVID-19 has increased sharply, accompanied by varying manifestations of disease. The basic pathogenesis of coagulopathy in COVID-19 accordance with Virchow's Triad theory which is consists of three pathological processes, namely endothelial injury/damage, hypercoagulable state, and stasis. Endothelial damage occurs due to direct invasion of the SARS-CoV-2 virus through the ACE2 receptor, the effects of pro-inflammatory cytokines, the release of various acute phase proteins, and activation of the complement system as well as the use of various intravascular catheters that stimulate local inflammation. Stasis conditions such as in patients with severe symptoms in the intensive care unit cause the flow in the blood vessels to not flow smoothly so that coagulation factors can concentrate in one location and then be activated and stimulate thrombosis. [10] In this study, clinically day off illness and survival date were significantly different in the two groups. All coagulation marker parameters increased in the severe group when compared with the non-severe Covid 19 group. These results aligned with previous studies.[11-14] Many patients infected with COVID-19 have mild or even no symptoms

and some patients develop severe and critical cases that lead to multi organ failure such as respiratory included and finally, death if not treated properly. Inflammation and immune system responses play an important role in the pathophysiology of COVID-19, this is characterized by a significant increase in levels of pro-inflammatory cytokines. [10] In COVID-19, local and systemic inflammations cause a hypercoagulable state that eventually will lead disrupt the balance of coagulation and fibrinolysis system. Hypercoagulation and hypofibrinolysis will trigger thrombosis in COVID-19 patients. Since a lot of ACE2 receptors are utilized by SARS-COV-2 to invade the human tissues, there is less ACE2 receptors available for angiotensin II (AT-II), and hence, more AT-II in the circulation. The virus and AT-II together will increase the production of plasminogen activator inhibitor 1 (PAI-1), which will establish a systemic pro-coagulant environment in the patients' circulation.[10] In COVID-19, identification parameters or markers to predict disease progression are very important. Coagulation parameters are one of the markers to predict this when the patient is admitted to the hospital. In this study, the median of aPTT in the two groups were not significantly different and normal. These results aligned with several previous studies conducted in China which showed similar results.[15] In the other hand, PT and INR in severe COVID-19 patients are significantly higher than the non-severe patients. Endothelial damage in COVID-19 exposes subendothelial tissue factor (TF) which will activate the extrinsic coagulation pathway. Furthermore, tissue factor pathway inhibitor (TFPI), which inhibits the extrinsic coagulation pathway, is impaired by COVID-19. These mechanisms may explain why PT and INR, depicting the extrinsic coagulation pathway, are affected more significantly than aPTT which depicts the internal coagulation pathway. [12] The median of fibrinogen levels in the severe COVID-19 patients in this study was higher than non-severe patients. Fibrinogen is one of acute-phase proteins synthesized by liver as response to stimulations from inflammatory cytokines and being involved in fibrin production in a final step of coagulation activity and its level is increasing in a hypercoagulable state.[13,14] The median of D-dimer in the severe group was significantly higher than the non-severe group. D-dimer is a specific cross-linked fibrin degradation product. D-dimer levels depict the process of fibrinolysis which will increase in a hypercoagulable state. D-dimer levels will increase as the severity of COVID-19 increases. D-dimer is one of the most established parameters used in monitoring hypercoagulable state in COVID-19.[12,14] The median platelet count of the two groups was still within normal limits. Several multicenter studies showed a higher incidence of thrombocytopenia in severe COVID-19 patients than in non-severe COVID-19 patients. The difference in the time of platelet count taken, either in the beginning or middle of hospitalization, could cause the difference between the results of this study and the previous studies.[15, 16]

Some potential confounding factors in this study, such as liver and kidney diseases, were not analyzed, so parameter values did not fully depict coagulopathy merely due to COVID-19. In conclusion, INR, PT, fibrinogen, and D-dimer values increased significantly in the severe COVID-19 group and can be considered to predict the severity of the disease and to choose the right treatment for COVID-19 patients. Briefly, the examination of INR, PT, fibrinogen, and D-dimer can be considered to predict the severity of the disease and to choose the right treatment for COVID-19 patients.

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Correlation between Acute Phase Symptoms with Neurological Long Covid Symptoms on COVID-19 Survivors

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Abstract

Objective: To investigate prolonged neurological impacts of COVID-19 and establish a connection between initial COVID-19 symptom severity and chronic fatigue syndrome (CFS) development, poor sleep quality (PSQ), and cognitive impairment (CI) in individuals recovered from COVID-19.

Methods: This cross-sectional study recruited COVID-19 survivors at Dr. Hasan Sadikin General Hospital Bandung, Indonesia, between June and December 2021. All participants gave informed consent and underwent interviews on demography, clinical features, long-COVID questionnaire, and neurological examination. Participants underwent cognitive examination (MOCA-INA), Chalder Fatigue Scale and Pittsburgh Sleep Quality Index (PSQI) to assess CI, CFS, and PSQ variables. Chi-Square analysis was performed to determine the probability of neurological long COVID-19 syndrome manifestations using SPSS 24.0.

Results: Of the 127 participants recruited, 67.7% were women, median (IQR) age of 33 (21–65) years, and time from hospitalization to examination of nine months (1–13). The most common neurological Long COVID symptoms were PSQ (59.8. %), CFS (51.2%), and CI (33.9%). Participants with more than five acute phase COVID-19 symptoms had a higher probability of CFS and CI (OR 2.38 (1, 16-4.9, CI 95%); OR 2.20 (1.01-4.79, CI 95%)) than those with less than five symptoms. The study did not find a significant correlation between sleep quality and number of acute-phase COVID-19 symptoms (OR 1.56 (0.76-3.20, CI 95%)).

Conclusion: Almost two-thirds of the COVID-19 survivors experienced PSQ, more than half had CFS, and almost one-third had CI. The study revealed an increasing likelihood of CFS and CI in COVID-19 survivors as the number of acute COVID-19 symptoms increases.

Keywords: Chronic fatigue syndrome, cognitive impairment, long covid, poor sleep quality

Introduction

COVID-19, also known as Coronavirus Disease-19, is an illness caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). Initially identified in Wuhan, China, in 2019, it rapidly spread to numerous countries, leading the World Health Organization (WHO) to declare a pandemic in early 2020. While the respiratory tract is primarily affected by this disease, it can also have an impact on various other organs, including both the central and peripheral nervous systems.[1] According to the World Health Organization (WHO) data available until May 2021, the global number of confirmed COVID-19 cases stood at 159 million, with a reported death toll of 3.3 million, resulting in a fatality rate of 2.1%. In the case of Indonesia, the COVID-19 death rate was higher than

the global average, reaching 2.7%.[2,3] The full range of health outcomes related to COVID-19 is still not completely understood. However, approximately 35% of individuals who have recovered from COVID-19 report not fully returning to their pre-illness state within 2–3 weeks after being declared cured. In cases where individuals have experienced severe pneumonia as a result of COVID-19, it may take six months or even longer for their breathing to return to normal. Furthermore, this prolonged disability can also affect the functioning of the heart and brain.[1,4] In neurology, many COVID-19 survivors report fatigue, sleep disturbances, and cognitive impairment symptoms. Patients with cognitive impairment tend to describe complaints of "brain fog," which causes behavioural fluctuations that can be frustrating for patients and healthcare professionals and fatigue. This situation is called "Long COVID." An additional factor to consider is whether, in the long term, chronic subclinical inflammation can lead to accelerated aging both peripherally and as a neurodegenerative process. [4]

The exact cause of "Long COVID" is still not fully understood, but it is believed to involve potential cellular damage caused by the virus itself and the ongoing production of inflammatory cytokines by the immune system, even after the virus is no longer present. Emerging evidence suggests that COVID-19 patients with Long COVID may experience brain injury, which aligns with the virus's ability to infect the central nervous system (CNS). However, the clinical manifestations, frequency of CNS effects, and specific mechanisms underlying the neurological damage caused by SARS-CoV-2 infection are not well-established and require further research. Therefore, the objective of this study was to provide an overview of the long-term neurological effects and explore the relationship between the number of acute-phase COVID symptoms and Long COVID symptoms in survivors of COVID-19.

Methods

This cross-sectional study was conducted at Neurology Outpatient Clinic in Hasan Sadikin Hospital, Bandung, Indonesia, between January – June 2022. We invited survivors of COVID-19 infection who had been hospitalized in this hospital during the period of June–December 2021. Inclusion criteria were (1) aged 18 to 65 years, (2) had confirmed COVID-19 infection based on reverse transcription real-

time polymerase chain reaction (RT-PCR) from nasal swabs, (3) had recovered from COVID-19, either confirmed negative by RT-PCR from nasal swabs, or had undergone mandated isolation period for a minimum of 14 days, (4) had undergone at least grade 3 Elementary School, (5) domiciled in the city of Bandung and its surroundings and (6) willing to complete questionnaires. Subjects with previous medical history (stroke, diabetes, cardiovascular disease, psychological disorders, and sleep disorder) were excluded from the study. The research ethical approval was obtained from the ethics committee of Hasan Sadikin Hospital (ethical clearance number: LB.02.01/X.6.5/231/2021). Global function examination with the Montreal Cognitive Assessment Indonesia (MoCA-Ina) is the value obtained by adding up all existing domains with a score range of 0-30, then grouped based on cognitive scores.[5] The questions examined visuospatial, executive function, naming, memory, attention, language, abstraction, delayed recall, and orientation. The measurement scale obtained is in the form of a categorical (ordinal) scale. Value of 24 or more is considered normal. Fatigue was evaluated by utilizing the Chalder Fatigue Scale (CFQ-11) survey, which consisted of 11 questions rated on a scale of 0 to 3.[6] The responses from these questions were combined to calculate a comprehensive score ranging from 0 to 33, with higher scores indicating more severe symptoms. Additionally, the questionnaire included two subcategories: physical exhaustion, comprising seven items with a potential score range of 0 to 21, and mental exhaustion, consisting of four items with a possible score range of 0 to 12. The Chalder Fatigue Scale (CFQ-11) offers an alternative scoring method called the bimodal score, where each item response is divided into two categories: 0 (0–1) or 1 (2–3). These scores are then summed up to create a scale ranging from 0 to 11. Typically, the fatigue case status, distinguishing between feeling tired or not tired, was determined using this scale. The conventional threshold for categorization was set at a score of <4 for not tired and 4 or above for feeling tired. Each participant fulfilled the Indonesian Version of Pittsburgh Sleep Quality Index (PSQI, Cronbach's alpha of 0.79) to assess the sleep quality in patients over a 1-month period. PSQI consists of 19 questions, which include sleep latency, duration, efficiency, disturbances, use of sleeping medication, and daytime dysfunction.[7] The questionnaire requires the patient to describe
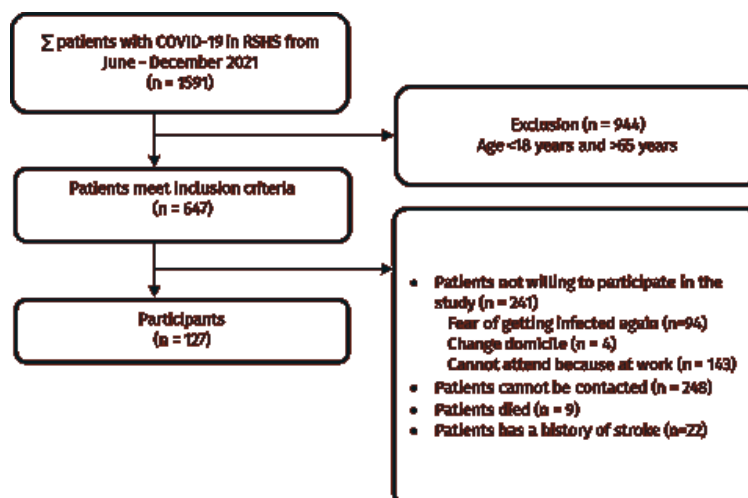
Fig. 1 Flow Chart of Participants

Table 1 Demographic Characteristics of Participants

Variables	(n=127) (%)	Median
Gender		
Male	41 (32.3)	
Female	86 (67.7)	
Age (years)		33 (21–65)
Body Mass Index (kg/m^2)		24.8 (16.2–43.5)
Underweight	4 (3.1)	
Normal	45 (35.4)	
Overweight	15 (11.8)	
Obesities	63 (49.6)	
Comorbidity		
Hypertension	11 (8.7)	
Diabetes	2 (1.6)	
Cardiovascular disease	4 (3.1)	
Chronic Obstructive Pulmonary Disorder	5 (3.9)	
Hypertension and Cardiovascular disease	3 (2.4)	
No comorbid	102 (80.3)	
Length of hospital stay (days)		14 (0–40)
ICU admission	5 (3.9)	
Length of ICU stay (days)		14 (7–20)
Time from discharge to follow-up (months)		9 (1–13)
CT Value		24 (11–38)
Number of acute phases of COVID symptoms		
≤5	54 (42.5)	
>5	73 (57.5)	

Note: Categorical characteristic data is displayed in terms of frequency and percentage, while numerical characteristics are displayed in the form of mean, standard deviation (SD), and range

sleep patterns, such as typical bedtime and wake time, length of time taken to fall asleep, and actual sleep duration. The patient then answers a series of questions relating to sleep habits and quality. Component scores ranges from 0-3. The possible total score is within the range of 0-21 with cut-off point for poor sleep quality is higher than 5. Statistical analysis was performed with SPSS version 24.0. The normally distributed variables were expressed as mean ± standard deviation and were compared by t-test. The skewed variables were expressed as medians (IQR) and were compared by using the Mann–Whitney U-test. The Chi Square test was used to determine the relationship between long COVID symptoms and the number of acute phases of COVID symptoms.

Results

From existing records, there were 1,591 patients with COVID-19 who were treated at RSHS from June to December 2021. 944 subjects did not fulfil age criterion, leaving 647 subjects eligible for the study. Of these 647 subjects, nine people had died, 22 had a history of stroke, 248 people could not be contacted/did not give an answer, and 241 people were not willing to take part in the study for the following reasons: (1) fear of re-infection (n=94); (2) change of domicile (n=4); and (3) unable to attend due to work (n=143), so that 127 patients were available for this study (Fig. 1).

The characteristics of the research subjects comprised 32.3% men and 67.7% women, with a median age of 33 years (range: 21 – 65 years), and almost 50% were obese. Most had no comorbidity (80.3%), and the most comorbid was hypertension (8.7%). The median length of stay was 14 days (range: 0 – 40 days); 3.9% were admitted to the ICU, with the median length of stay in the ICU being 14 days. The median CT-value is 24 (range (11 –38)). Based on the number of symptoms of the acute phase of COVID, subjects who had symptoms >5 were 57.5%, and 5 were 42.5%. The basic characteristics of the research subjects can be seen in Table 1.

The median time to go home / be declared cured until the examination was nine months (range 1–13 months). All subjects completed the Long COVID questionnaire and obtained the most neurological symptoms, namely fatigue (53.9%), sleep disturbances (26.8%), muscle weakness (22.8%). Other symptoms such as joint pain, headache, myalgia, dizziness,

Table 2 Characteristics of Long COVID Symptoms in Participants

Variables	Total (n=127)
Long COVID symptoms, n (%)	
Fatigue	68 (53.9)
Headache	9 (7.1)
Myalgia	4 (3.1)
Chest pain	2 (1.6)
Joint pain	10 (7.9)
Sore throat	5 (3.9)
Difficult to swallow	2 (1.6)
Low grade fever	5 (3.9)
Palpitations	8 (6.3)
Dizziness	6 (4.7)
Nasal congestion	5 (3.9)
Skin rash	5 (3.9)
Diarrhea or vomiting	6 (4.7)
Nausea	6 (4.7)
Smell disorder	11 (8.7)
Taste disorder	6 (4.7)
Decreased appetite	4 (3.1)
Sleep difficulties	34 (26.8)
Muscle weakness	29 (22.8)
Hair loss	41 (32.3)

Note: Categorical variables of Long COVID symptoms are displayed in the form of frequency (%)

olfactory disturbances, and taste disturbances were found in less than 10% of the subjects (Table 2).

The analysis results in Table 3 showed that subjects who had > 5 symptoms of acute phases COVID symptoms had more cognitive impairment than thos who had < 5 symptoms (41.1% vs 24.1%, OR: 2.20; 95% CI: 1.01–4.79; p=0.045). Chronic fatigue syndrome was also more frequently found in subjects with >5 symptoms in the acute phase of COVID-19 (60.3 vs 38.9, OR: 2.38; 95% CI: 1.16–4.90; p=0.017). there were no significant statistical difference between those two groups with regard to sleep disturbance (Table 3).

Discussion

The study's results on 127 patients showed that COVID-19 was more common in women,

Table 3 Correlation between Cognitive Disorders, Chronic Fatigue Syndrome, and Sleep Disorders (categorical) based on the Number of Symptoms of COVID-19 in the Acute Phase

Long COVID	Total n=127	Number of Symptoms of COVID-19 in Acute Phase		p-value	OR (95% CI)
		>5 n=73	≤5 n=54		
MOCA-INA					
Cognitive impairment	43 (33.9)	30 (41.1)	13 (24.1)	0.045*	2.20 (1.01 – 4.79)
Normal	84 (66.1)	43 (58.9)	41 (75.9)		
Chalder Fatigue Scale,					
Chronic Fatigue Syndrome	65 (51.2)	44 (60.3)	21 (38.9)	0.017*	2.38 (1.16 – 4.90)
Normal	62 (48.8)	29 (39.7)	33 (61.1)		
PSQI					
Poor Sleep Quality	76 (59.8)	47 (64.4)	29 (53.7)	0.225	1.56 (0.76 – 3.20)
Normal	51 (40.2)	26 (35.6)	25 (46.3)		

Note: analysis using Chi-Square test, *p<0.05

which was 67.7%. This result is supported by similar results obtained in several other studies, which show that more women suffer from COVID-19 than men, with a relatively small percentage of 69%, 63%, and 52%.[8,9,10] The study of Francesca Bai *et al*.[11] also revealed that women have a 3-fold higher risk of being diagnosed with Long COVID. Hormones may play a role in maintaining a hyperinflammatory state during the acute phase even after recovery, and more robust IgG antibody production in women in the early stages of the disease has been reported; this may result in a more favorable outcome in women, but may also play a role in prolonging the manifestations of the disease.The patients in this study had a median of 33 years. Several similar studies showed variations in the median age of patients suffering from Long COVID-19, namely 33, 36.5, and 39.35 years.[8,12,13] Nearly 50% of the patients in this study were obese. Obesity is associated with chronic inflammatory conditions and a reduced immune system, increasing a person's susceptibility to infection. Therefore, obesity is an independent risk factor for the poor progression of COVID-19 disease. The mechanisms associated with disease severity in obesity are thought to occur through higher ACE-2 concentrations, chronic inflammation, and the restrictive functional capacity of the obese lung.[14] The comorbidity most often accompanies patients with COVID-19 is hypertension, which is 8.7%. Meanwhile, Huang *et al*.[16] in their study showed a higher percentage (29%) of hypertension, and research by Sanyaolu *et al*.[15] proved that hypertension was the most common comorbid (15%) in patients diagnosed with COVID-19. The investigators agree that subjects with comorbidities were associated with more severe disease outcomes when infected with SARS-CoV-2 compared to patients without previous comorbidities.[16]

This study collected data on the number of symptoms experienced by patients suffering from acute COVID-19 and the symptoms experienced by patients after being declared cured of COVID-19, including those involving neurological sequelae, with the most common symptoms being excessive fatigue, cognitive impairment, and sleep disorders.

This study results are in line with several previous studies, including those from the United States, Europe, and China, which reported the outcome of patients who had completed hospitalization in the acute phase of COVID-19. COVID-19 survivors are reported to have some persistent symptoms. In a study in the United States, 32.6% of patients still had symptoms, 55% in Europe and 76% in China. The most frequently reported symptoms were fatigue (98%), shortness of breath (93%), and headache (91%). However, many symptoms still affect other systems in the body and fluctuate from time to time. A review article of 27 studies on the post-COVID-19 syndrome showed that the most common symptoms were fatigue (47%), shortness of breath (32%), and muscle aches (25%). The study

of Graziella Orru *et al.* on the persistence of neurological and psychological symptoms also showed similar results, where the main symptoms associated with Long COVID were headache (90%), fatigue (80%), muscle pain/myalgia (70%), articular pain (55%), cognitive impairment (59%), loss of smell (55%), and sleep disturbances such as insomnia (26%).[17,18,19] Long COVID-19 syndrome is a complication with persistent symptoms after recovery from SARS-CoV-2 infection. Guidelines published by the National Institute for Health and Care Excellence (NICE), The Scottish Intercollegiate Guidelines Network, and the Royal College of General Practitioners define long COVID-19 as signs and symptoms that develop during or after COVID-19-related illness and persist for more than four weeks without being supported by another diagnosis. Two main symptom groups of long COVID have been identified: (1) a group consisting only of fatigue, headache, and upper respiratory tract complaints; and (2) the group with multi-system complaints including fever and gastroenterological symptoms.[20,21] Studies linking the number of symptoms experienced during acute conditions with long COVID-19 have been carried out previously. According to Sudre *et al.*,[21] more than five symptoms in the first week of acute infection were significantly associated with the development of long COVID-19 regardless of age or gender. In this study, long COVID symptom indicators were expressed by several scoring systems for cognitive impairment, CFS, and sleep disorders.

As assessed by the Chalder Fatigue Scale, the number of acute phase COVID-19 symptoms was significantly associated with CFS. A study by Stavem *et al.* also demonstrated that CFS rates were higher in patients with severe symptoms during acute COVID-19 based on three different scoring systems. The study's results by Goertz *et al.*[22] also support this finding by suggesting that the number of symptoms present during initial infection was the most potent factor in predicting the number of symptoms at three months.[23] Chronic fatigue syndrome is defined as fatigue, post-activity malaise, sleep disturbance, cognitive impairment, and persistent unprovoked pain lasting six months or more of sufficient intensity, not fully explained by any medical condition. This condition can be observed after some viral and bacterial infections. There is also an association between CFS and depression, although it remains unclear whether one diagnosis precedes the onset of

another.[24] Symptoms of CFS can be caused by damage to multiple organ systems during the acute phase of COVID-19, causing impaired heart, lung, or kidney function. The overall inflammatory state increased inflammatory mediators, and activation of cell-mediated immunity may contribute to a CFS-like state. Disruption of routine activities due to ongoing post-COVID-19 draining symptoms, social isolation, and post-traumatic syndrome due to severe illness requiring mechanical ventilation can lead to depression, which can sometimes trigger CFS. Furthermore, endocrine dysfunction leading to hypocortisolism, hypothyroidism, or disruption of the hypothalamus-pituitary-adrenal (HPA) axis may also be another potential explanation for CFS.[24] In this study, it was found that there was a significant relationship between the number of acute phase COVID-19 symptoms and cognitive impairment as measured by MoCA-Ina. This result is similar to that was observed by Jessica *et al.*, who did a follow-up of up to 12 months on 96 COVID-19 survivors and found that only 22.9% of patients were completely symptom-free, and one of the symptoms persisted until the 12th month was neurocognitive symptoms. The cause of some patients experiencing long-term symptoms after COVID-19 remains unclear, but a potential cause for differences in post-infection outcome is viral load and host factors such as genetic susceptibility or induction of anti-inflammatory cells. The development of IgA ANA autoantibodies and high titers of serum IgG antibodies targeting the GD1b ganglioside have been found in certain neurologic affected patients. A study by Miskowiak *et al.*[25] observed the trajectory of cognitive functions from 3 months to 1 year after hospitalization with COVID-19, indicating that patients with impaired cognition three months after hospitalization do not improve after one year, while patients with no impairments after three months remain cognitively normal. This is consistent with meta-analytic analysis by Ceban *et al.* that suggested that patients' cognitive impairments after COVID-19 persist over time. However, this is contradicted by the results of a study conducted by Alemanno *et al.*, who reported a high prevalence of cognitive impairment during the acute phase of COVID-19; examination at follow-up one month after discharge found that the total MoCA and Mini-Mental Status Examination (MMSE) scores were significantly higher than at admission. This indicates that cognitive impairment is more severe during the

acute phase of COVID-19 than in the acute post-COVID-19 phase.[26] This study found that COVID-19 survivors with some acute phase COVID symptoms >5 experienced sleep disturbances but were not statistically significant. Several previous studies have shown that the number of symptoms of the acute phase of COVID is associated with decreased sleep quality in COVID-19 survivors. The increased number of symptoms of the acute phase of COVID is closely related to the severity of COVID. The severity of COVID-19 is related to a cytokine storm mediated by IL-6, thereby increasing the permeability of the blood-brain barrier causing activation of glial cells, producing inflammatory cytokines, and resulting in sleep disturbances. In this study, the results were not statistically significant, possibly because the cutoff score for the PSQI was too low. The study of Fernández-de-las-Peñas *et al.*[26] in Spain with a Caucasian population getting a PSQI cut of 8 showed a statistically significant difference in sleep quality in Long COVID patients. Vitale *et al.*[28] conducted a study on four COVID-19 survivors that aimed to objectively assess the consequences of the severity of COVID-19 on sleep quality using actigraphy. Research subjects who experience severe COVID-19 degrees and require extended ICU care have the potential to affect sleep quality results, so it is concluded that there is a relationship between ICU care and poor sleep quality. On the other hand, the administration of necessary sedation during mechanical ventilation may play a role in decreasing sleep quality and disrupting sleep habits. Meanwhile, COVID-19 survivors treated in the ICU in this study were only 3.9%, so it did not produce a significant relationship.[23,24,25]

There are some limitation in this study. First, PSQI is a subjective questionnaire, so objective sleep measures are necessary to make a definite diagnosis and to clarify the presence/absence of other sleep disorders causative for participants' subjective disturbance in sleep maintenance. Second, this study assessed cognitive impairment using MOCA-INA as a screening tools that could not describe the specific cognitive subdomain in Long COVID. Third, this study did not collect laboratory data (cytokines, d-dimer, CRP, fibrinogen, procalcitonin) for patients during the acute phase of COVID. This study shows that almost two-thirds of COVID-19 survivors at this hospital experienced sleep quality disorders, more than half experienced chronic fatigue syndrome, and almost a third experienced cognitive disorders. There is a significant relationship between the number of symptoms of more than five during the acute phase of COVID-19 with chronic fatigue syndrome and cognitive impairment. Sleep disturbances were more common in COVID-19 survivors with more than five acute-phase COVID symptoms but were not statistically significant.

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Crowned Dens Syndrome: A Rare Cause of Sudden Onset Neck Pain

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Abstract

Objective: To report a case of Crowned Dens Syndrome (CDS), which is a rare disorder caused by crystal deposition by calcium pyrophosphate dihydrate in the peridontoid soft tissues surrounding the C1 and C2 vertebrae that presents in elderly with sudden onset neck pain, neck stiffness, fever, and elevated inflammatory markers, with periodontal calcification in a halo or crown configuration on radiography considered diagnostic.

Methods: A 64-year-old diabetic and hypertensive female patient presented with a 6-day history of sudden onset posterior neck pain and stiffness. Movements of the cervical spine were equally limited in all directions, causing marked aggravation of pain. There was no focal neurologic loss. Her inflammatory markers were markedly raised.

Results: Based on radiography, she was diagnosed with Crowned Dens syndrome and started on oral prednisolone, paracetamol, and tizanidine along with topical diclofenac. Oral NSAIDs were contraindicated due to her renal insufficiency.

Conclusion: Crowned Dens Syndrome (CDS) is a rare cause of neck pain. Clinicians should consider this syndrome in their differential diagnosis. Timely diagnosis and treatment of CDS will lead to avoidance of unnecessary investigations and medications in such patients, along with a reduction in the length of stay.

Keywords: Calcium pyrophosphate deposition, crowned dens syndrome, neck pain, neck stiffness

Introduction

Crowned Dens Syndrome (CDS) is a rare disorder and was first reported in 1985 as a disorder occurring mainly in older individuals having a male-to-female ratio of 3:5. An under-recognized cause of acute neck pain and fever, CDS is a distinctive clinical syndrome linked to Calcium Pyrophosphate Deposition Disease (CPPD). CPPD, occurring mostly in articular cartilage and ligaments, is asymptomatic in 50% patients but can manifest as acute joint inflammation similar to gout, and is therefore also referred as pseudogout. CDS is caused by crystal deposition by calcium pyrophosphate dehydrate in the peridontoid soft tissues surrounding the C1 and C2 vertebrae. It generally presents in elderly with sudden onset neck pain, neck stiffness, fever and elevated inflammatory markers.[1,2] Delirium has also been reported in these elderly patients. CDS is a rare entity and little is known about its epidemiology. It is very likely that many cases of CDS are missed. Its diagnosis relies heavily on appropriate imaging. Diagnosis of CDS is based on presence of periodontal calcification above and lateral to dens of C2 vertebra in a halo or crown conFig.uration on radiography.[3] Aspiration of local fluid collections that demonstrate calcium pyrophosphate crystals in crowned dens syndrome is the most definite means for diagnosis but aspirations are rarely performed clinically.[4] Advances in imaging for example dual-energy computed

tomography, that may chemically identify crystal deposition, would certainly help in CDS diagnosis.[5] But until such type of testing becomes easily available, it is essential that CDS be included as a differential diagnosis in clinical evaluation of patients with acute neck pain and raised inflammatory markers especially in elder patients.

CDS generally required medical management with anti-inflammatory medications alone being the mainstay of treatment.[6] CDS has a good prognosis and the patients generally become asymptomatic within 4–6 weeks after initiation of therapy.[7] Majority of the patients recover without any clinical sequelae. Modification or resorption of the calcific deposits is commonly seen within 4-6 weeks or even earlier. Non-steroidal anti-inflammatory drugs (NSAIDs) are the gold standard of anti-inflammatory treatment in CDS and are given as first line therapy. NSAIDs provide rapid relief of pain generally within a few days after initiation and also reduce the blood inflammatory markers. Oral colchicine may also be prescribed in addition to NSAIDs. In severe disease or disease not responding to NSAIDs, corticosteroids such as prednisolone may be used. Furthermore, in refractory or severe cases where the symptoms persist despite medical therapy, surgical decompression and stabilization may be required, especially when there is evidence of spinal cord compression, myelopathy or cervical stenosis.[8] Herein, the report case of a patient presenting with sudden onset posterior neck pain and stiffness who was diagnosed with CDS after appropriate radiography. Although a rare cause of neck pain, it is important to diagnose CDS timely and clinicians should consider it in their differential diagnosis to avoid unnecessary investigations and medications in such patients.

Case

A 64-years old female patient presented with 6-day history of sudden onset posterior neck pain and stiffness of moderate to severe intensity causing difficulty in neck movements. There was no history of trauma. She was a known diabetic and hypertensive for last 15 years, taking oral medicines with good compliance and good control. On examination, the patient was vitally stable with a temperature of 100°F (37.7°C). She was apprehensive due to pain but was co-operative and reported tenderness on palpation of back of neck. There were no deformity, mass or skin lesions on examination of neck and back. Movements of the cervical spine were equally limited in all directions, with no radiation of pain. However, neck movements caused marked aggravation of pain. Signs of meningeal irritation (Kerning's and Brudzinski's) were negative. There was no sensory loss; normal muscle tone, reflexes and power in both upper and lower limbs. Rest of the examination was unremarkable.

The X rays of the cervical spine demonstrated calcification of para-vertebral
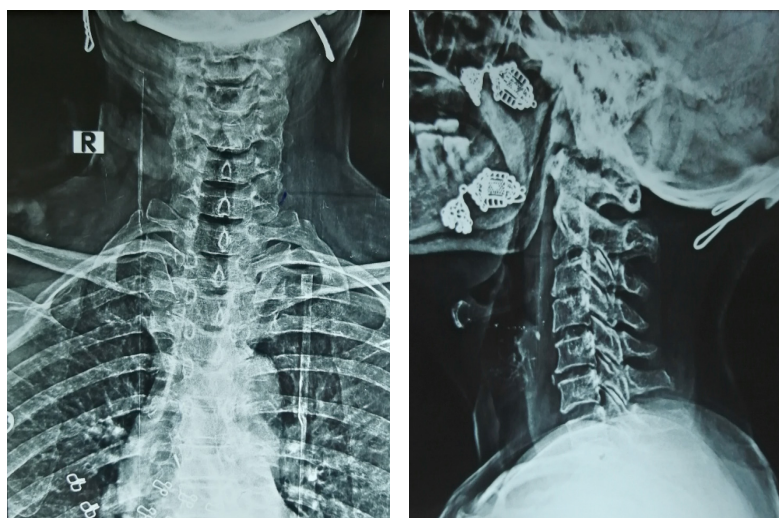
Fig. 1 X-ray Cervical Spine (AP and Lateral Views)

Fig. 2 X-ray Hands (AP and Oblique views)

soft tissue at C1 and C2 vertebrae, mild osteophyte formation and straightening of cervical spine as shown in Fig. 1. On further investigation, her ESR (98 mm/hour) and CRP (86 mg/dl) were markedly raised. She had moderate renal insufficiency with a creatinine clearance of 45 ml/min. Her CBC, liver profile and urinalysis were normal. HbA1c was 6.6%. Blood and urine cultures were negative. X rays of the hands demonstrated minimal joint space narrowing at 3rd and 4th PIP joints bilaterally, subtle osteophyte formation at right 3rd PIP joint and generalized reduction in bone mineral density as shown in Fig. 2.

The X rays of the knees demonstrated moderate joint space narrowing of medial compartment more of left knee and early osteophyte formation as shown in Fig. 3. The differential diagnosis included cervical spondylitis, vertebral fracture, metastatic vertebral tumor, meningitis, polymyalgia rheumatic and giant cell arteritis which were ruled out after clinical examination and investigations. Based on clinical and radiographic findings, she was diagnosed as Crowned Dens syndrome and started on oral prednisolone 10mg per day, colchicine 1mg per day, paracetamol 2gms per day and tizanidine 8mg per day along with topical diclofenac gel application. Oral NSAIDs were contraindicated due to her renal insufficiency. The patient improved and was discharged 7 days after admission with advice regarding regular follow up and tapering of oral corticosteroids.

Discussion

CDS is a rare cause of neck pain, stiffness,
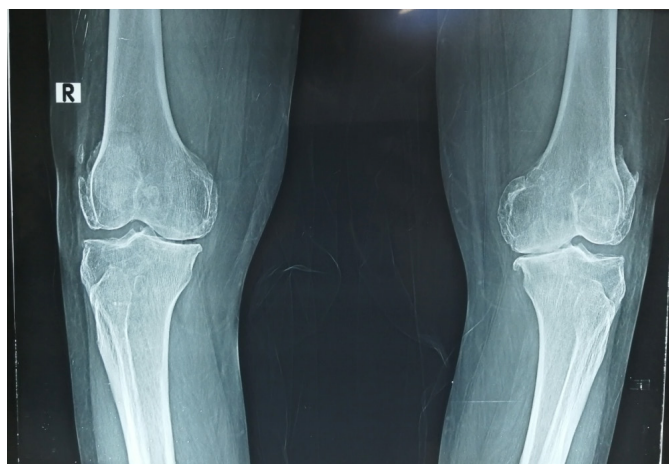
Fig. 3 X-ray Knees (AP view)

fever and elevated inflammatory markers. The differential diagnosis of neck pain, stiffness and fever is quite broad and includes cervical spondylitis, vertebral fracture, metastatic vertebral tumor, meningitis, polymyalgia rheumatic and giant cell arteritis.[9] There is often a delay in diagnosis of CDS or it may be misdiagnosed entirely leading to extensive investigations, inappropriate medications and prolonged hospital stay.[9,10] CDS is not uncommon but is often misdiagnosed or ignored due to a lack of knowledge about the disease. Statistics suggest that CDS is a major cause of acute neck pain causing limited mobility accounting for up to 2% cases of acute neck pain.[11] However with adequate clinical finding and appropriate investigations the differential diagnosis may be ruled out and a diagnosis of CDS can be made timely. The current diagnostic criteria for CDS include a history of acute neck pain and limited cervical activity in addition to raised inflammatory markers such as ESR, CRP and white blood cells. Radiographic finding of CDS is presence of periodontal calcification above and lateral to dens of C2 vertebra in a halo or crown conFig.uration.[3] The limitation of X-rays is that anatomical structures surrounding odontoid process are not distinguished separately. CT scan is considered investigation of choice to identify calcification of the periodontal ligaments especially the transverse ligament of atlas cruciform ligament, apical ligament and alar ligament.[12] MRI scan does not help to diagnose calcification but is superior to see inflammatory response and spinal cord compression.[13] The definitive diagnosis relies on histological demonstration of calcium pyrophosphate crystals on biopsy.[14] However the current patient was needle phobic and refused aspiration biopsy. The incidence of CDS is associated significantly with sex and age being more prevalent in elderly females.[11,15] Oka et al.[16] reported that patients with CDS had a mean age 71.4 years with 60% female preponderance. Trauma, genetic factors and the co-presence of rheumatologic diseases may affect development of CDS.[11] However, there has been no proven relationship of CDS with diabetes or hypertension. Calcium Pyrophosphate crystal deposition in peripheral joints can lead to chondrocalcinosis and early osteoarthritis of these joints.[17] Performing radiographs of peripherals joints (knee, hands, and wrist) in absence of specific symptoms may demonstrate involvement of joints other than atlantoaxial joint in CDS patients. In the current patient, there was no radiographic evidence of chondrocalcinosis in joints of hands, wrists and knees. This is similar to the case reported by Lee et al.[18] CDS has a good prognosis and the patients generally improve with medical management encompassing anti-inflammatory drugs (NSAIDs, corticosteroids, colchicine).[19,20,] The current patient had renal insufficiency due to which NSAIDs were contraindicated. She was started on oral prednisolone 10mg per day and colchicine 1mg per day after which she reported improvement in her symptoms. Follow up was planned with an aim to taper and stop colchicine in 2 weeks and corticosteroids in 4 weeks.

In conclusion, Crowned Dens Syndrome (CDS) is a rare cause of neck pain and should be considered by clinicians in their differential diagnosis. Timely diagnosis and treatment of CDS will lead to avoidance of unnecessary investigations and medications in such patients along with a reduction in length of stay.

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Case Report

Paradoxical Hemiparesis from Cerebellopontine Angle Tumor: A Case Report

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Abstract

Objective: To report a vestibular schwannoma in the cerebellopontine angle presenting with paradoxical hemiparesis with the Kernohan-Woltman Notch Phenomenon (KWNP).

Methods: A 31-year-old female presented to the neurology clinic at Bhayangkara Hospital TK. I R. Said Sukanto, Indonesia, on 29 November 2021 with loss of balance, hearing, vision, and weakness in her left arm and leg. On physical examination, the patient had reduced left arm and leg muscle strengths against resistance (MRC grade 4), face deviation to the left, abnormal finger-to-nose test, dysdiadochokinesia, and inability to perform tandem gait. She was admitted for a brain MRI but did not return to the hospital for re-evaluation and surgery.

Results: The brain MRI showed a mass on the left side of the cerebellum with a size of 4.44x3.93x4.93 cm, suggesting vestibular schwannoma. The mass also caused the obliteration of the ventricle, causing hydrocephalus.

Conclusion: KWNP is an unusual finding resulting in a paradoxical hemiparesis, a false-localizing neurologic sign. Physicians should recognize KWNP in patients with hemiparesis, especially in space-occupying lesions. Imaging studies can help localize the lesion to minimize misdiagnosis and optimize patient treatment.

Keywords: Cerebellopontine angle, kernohan-woltman notch phenomenon, paradoxical hemiparesis, vestibular schwannoma

Introduction

Expanding intracranial lesions occasionally produce focal neurological signs unrelated to the lesion's location. These paradoxical clinical signs are described as "false-localizing signs".[1-4] Kernohan-Woltman notch phenomenon is a false-localizing neurologic sign presenting with hemiparesis ipsilateral to the primary lesion.[5] This phenomenon occurs during transtentorial herniation, which causes the contralateral cerebral peduncle to be compressed against the free edge of the tentorium, thus causing compression of descending corticospinal tract fibers.[5-7] Furthermore, the Kernohan-Woltman notch phenomenon is considered an unusual finding. This article describes a patient with a space-occupying lesion of the cerebellum complaining of ipsilateral hemiparesis. This study aim to report a vestibular schwannoma in the cerebellopontine angle presenting with paradoxical hemiparesis with the Kernohan-Woltman Notch Phenomenon (KWNP).

Case

A 31-year-old female presented to the Neurology Clinic at Bhayangkara Hospital TK. I R. Said Sukanto on 29 November 2021 with a loss of balance since nine months ago. There was no history of trauma or falls. The patient also complained about loss of hearing, vision and weakness in the left arm and left leg. Past medical history was unremarkable, and the patient was on no medications. On
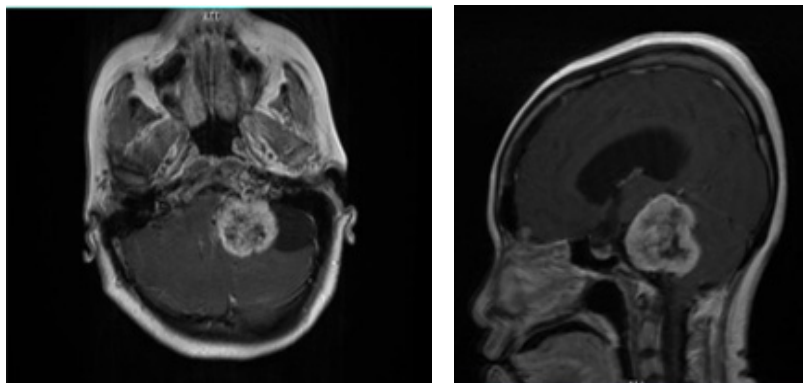
Fig. 1 CPA Mass in Magnetic Resonance Imaging, (A) Axial View, (B) Sagittal View

examination, she was hemodynamically stable, with reduced left arm and leg muscle strength against resistance (Medical Research Council (MRC) grade 4), deviation of the face to the left, reduced hearing function, and loss of balance. There was also abnormality in finger-to-nose test, dysdiadochokinesia, and inability to perform tandem gait. The patient was then admitted for brain magnetic resonance imaging (MRI) which showed a mass in the left cerebellopontine angle (CPA) with a size of 4.44 cm x 3.93 cm x 4.93 cm, suggesting vestibular schwannoma (Fig.1). The mass also caused the fourth ventricle to be obliterated causing hydrocephalus. In this case, the CPA mass could cause the left cerebral peduncle to be compressed, causing a disruption of the descending corticospinal tract. Thus, the patient had a left hemiparesis. The patient did not return to hospital for re-evaluation and surgery.

Discussion

Supratentorial lesions commonly cause neurological impairment of movement on the contralateral side of the body, which results from contralateral corticospinal projections. [7] These projections arise from cortical regions of the brain and decussate in the caudal medulla, then continue traveling down the spinal cord.[8] Almost all fibers decussate, resulting in contralateral clinical findings.[8] However, in a patient following hemorrhage, tumor, abscess, or infarction with brain swelling, a lateral and downward displacement of subthalamic-upper brainstem structures and herniation of the medial part of the temporal lobe into the opening in the tentorium usually occurs in large, destructive or space-occupying lesions. [3] The upper midbrain is pushed against the tentorium's contralateral edge, causing weakness and a Babinski sign ipsilateral to the hemispheral lesion known as the Kernohan-Woltman notch phenomenon (KWNP). [3] KWNP is one of the causes of false localizing neurological signs, manifesting with an ipsilateral neurological deficit and defying the corticospinal decussation principles.[9] Kernohan and Woltman propose the mechanism in which the descending pressure caused the squeezing of the cerebral crus's opposite side against the cerebellum's tentorial edge.[10,11] Based on MRI and CT studies by Carrasco *et al.*,[12] direct pressure of the cerebral peduncle from the tentorium would lead to the degeneration of myelinated fibers of the corticospinal tract, which leads to hemiparesis. The corticospinal tract controls voluntary movements for the somatic motor system from the neck to the feet. [13] This tract carries impulses from the primary motor cortex through the internal capsule, cerebral peduncles, and ventral pons, then decussate to the contralateral via the pyramidal decussation.[13]

The false localizing sign of KWNP can cause several diagnostic difficulties in the clinical setting, including operating on the wrong side of the hematoma, requiring neuropsychological testing to localize the lesion, and a case of tetraparesis leading to a misdiagnosis of consciousness.[4] CPA is a subarachnoid space located in the ventral surface of the brainstem and medial cerebellar hemisphere, bordered laterally by the superior and inferior limbs of the cerebellopontine fissure. Medially at the CPA, the lateral recess of the fourth ventricle opens to the CPA through the foramen of Luschka.[14] Tumors found in this region are

usually vestibular schwannoma, also known as acoustic neuroma, which accounts for 90% of the cases, meningioma (3%), primary cholesteatoma, and facial nerve schwannoma.[15] Tumors in the CPA usually present with signs and symptoms resulting from compression of cranial nerve V, VII, VIII, and lateral aspect of the pons and cerebellar peduncle, which depends on the size and extension of CPA tumors.[15,16] This patient, the findings from an MRI scan suggested a vestibular schwannoma in the left CPA. The patient complained about left-side hemiparesis, right facial palsy, hearing loss, and loss of balance. Surgical approaches for vestibular schwannoma include the retrosigmoid, middle fossa, and translabyrinthine approach.[17] In 208 cases described by Rauniyar et al.,[18] the most common complication of patients undergoing the suboccipital retrosigmoid approach was hearing loss (50%), facial nerve palsy (10.09%), and hydrocephalus (8.65%).The middle fossa approach needs to be more utilized compared to the retrosigmoid and translabyrinthine approaches. In an article by Raheja et al.,[19] the outcome of 78 patients undergoing the middle fossa approach was generally good, with good functional preservation of the facial nerve (90%), 75.5% with class A/B Association of Otolaryngology-Head and Neck Surgeons (AAO-HNS) hearing class, and no cerebrospinal fluid (CSF) leak, postoperative seizure, and dysphasia. Only three patients reported wound infections. Lastly, the translabyrinthine approach is a practical surgical approach for vestibular schwannoma. In a retrospective study from 1996 to 2017 by de Boer et al.,[20] a total of 596 with vestibular schwannoma underwent surgery with a translabyrinthine approach. The facial nerve function is preserved in 509 patients (85%) according to House-Brackmann (HB) grading system with a score of HB 1–2. Postoperative complications that can occur are CPA hematoma, meningitis, CSF leak, and wound infection. De Boer et al.[20] also points out that preoperative tumor size is the predictor for postoperative facial palsy.

In conclusion, KWNP is an unusual finding resulting in a paradoxical hemiparesis, a false-localizing neurologic sign. Physicians should be aware of KWNP in a patient with hemiparesis, especially in the setting of space-occupying lesions. Imaging studies can help to localize the lesion to minimize the misdiagnosis and optimize the treatment of the patient.

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