

Comparison of Serum Bile Acid Concentrations Between Maltese and Other Breeds of Dogs With Portosystemic Shunt

DONGWOOK KIM¹, HYEJONG OH¹, HEESOO AHN¹, BYOUNGHO AN¹,
DONGSUN PARK², KI-JEONG NA¹ and GONHYUNG KIM¹

¹Veterinary Teaching Hospital, College of Veterinary Medicine,
Chungbuk National University, Cheongju, Republic of Korea;

²Department of Biology Education, Korea National University of Education, Cheongju, Republic of Korea

Abstract. *Background/Aim:* Congenital portosystemic shunt (PSS) is a vascular anomaly forming a direct communication between portal and central venous systems, thus bypassing the liver. This condition is related to various clinical symptoms including those manifesting in the central nervous system, gastrointestinal tract, and urinary tract. Treatment of PSS includes medical management and surgery. When evaluating prognosis of dogs with PSS, serum biochemistry profiles including serum bile acid (SBA) and ammonia concentrations are routinely used as screening tests. However, the use of SBA concentration in Maltese is controversial because it can be measured above the reference range even in normal dogs of this breed. In addition, utilizing SBA levels to assess surgical prognosis of PSS is not widely understood in this breed. Thus, the present study evaluated whether SBA could be used as a screening test for PSS in Maltese dogs. *Materials and Methods:* Medical records of dogs in the Veterinary Teaching Hospital from 2018 to 2020 were retrospectively reviewed. *Results:* A total of 23 dogs with PSS and 30 Maltese dogs without PSS were analyzed. Although preoperative SBA levels were significantly higher in Maltese dogs (192 $\mu\text{mol/l}$) than in other dog breeds (137 $\mu\text{mol/l}$) with portocaval shunt, its concentrations were significantly decreased after surgery in both Maltese and other breeds of dogs. No significant difference was observed in postoperative SBA levels between

Maltese and other dog breeds. The mean SBA levels for Maltese dogs without PSS (8 $\mu\text{mol/l}$) were within the reference interval (0-25 IU/l). *Conclusion:* Measuring pre- and post-operative SBA levels to evaluate prognosis of PSS might also be available for Maltese.

Congenital portosystemic shunt (PSS) is a vascular anomaly first reported in human medicine as Abernethy malformation in 1793 (1). An aberrant vessel occurs secondary to abnormal development of fetal vasculature, thus forming a communication between the portal vein and venous systemic circulation (2). This abnormal condition is related to significant complications such as encephalopathy and hepatopulmonary syndrome (1). PSS has also been reported in veterinary medicine (3, 4). Havanese, Yorkshire Terrier, and Maltese are known as PSS-predisposed breeds (5). Clinical signs of PSS are generally associated with the central nervous system, gastrointestinal tract, and urinary tract (3). Diagnosis of congenital PSS is routinely made by radiography and ultrasound combined with blood tests (4, 6). Computed tomography (CT) is a useful tool to identify insertion site of the shunt as prognosis varies between shunt types (6). Treatment of PSS includes medical treatment and surgery (7). Medical management consists of dietary, antimicrobial, and lactulose treatments (7, 8). Surgical attenuation or closure of the shunt is made by using ameroid ring constrictor (ARC), cellophane band, or silk suture (9, 10). When evaluating pre- and post-operative prognosis for surgically treated shunts, serum bile acid (SBA) and ammonia concentrations are useful screening tests (4). Although a previous study documented that dogs with PSS can show higher SBA levels than normal dogs despite surgical ligation of the shunt (11), SBA is generally identified as a sensitive factor in evaluation of PSS (4, 12). When utilizing SBA for PSS evaluation, Maltese can be an exception as normal Maltese often show SBA levels above the reference interval (RI) (13). SBA concentration is therefore often not used as a routine test for PSS in this

Correspondence to: Gonhyung Kim, DVM, Ph.D., Department of Veterinary Surgery, College of Veterinary Medicine, Chungbuk National University, Cheongju 28644, Republic of Korea. Tel: +82 432613171, Fax: +82 432613224, e-mail: ghkim@cbu.ac.kr

Key Words: Portosystemic shunt, liver, bile acid, Maltese, dog.



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC-ND) 4.0 international license (<https://creativecommons.org/licenses/by-nc-nd/4.0>).

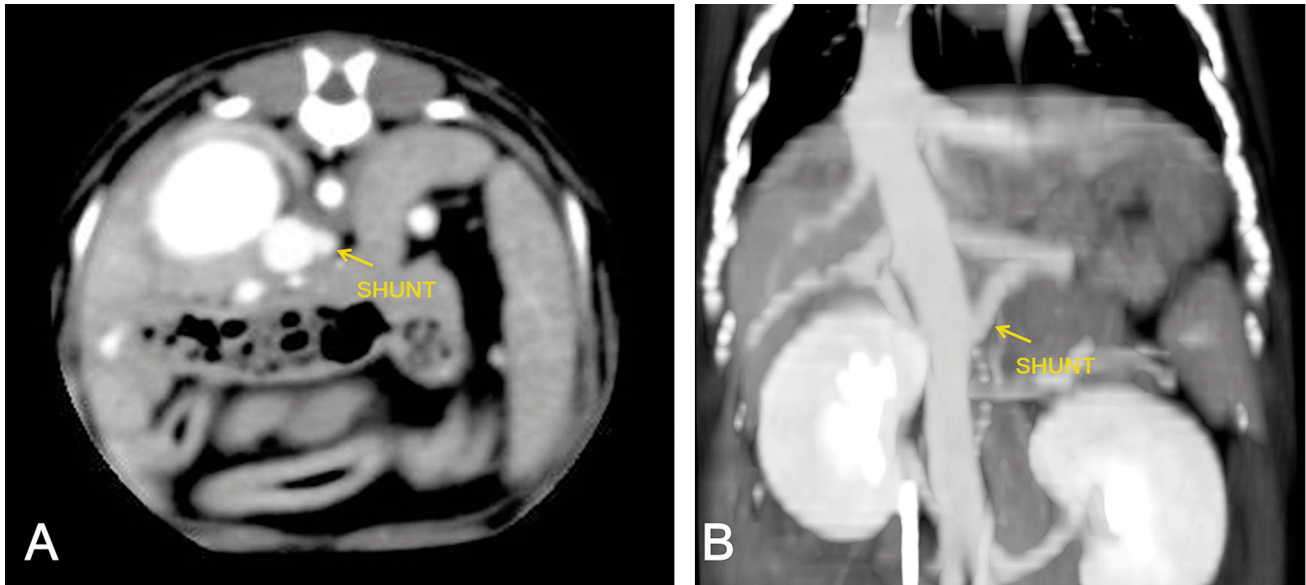


Figure 1. Transverse (A) and sagittal (B) computed tomography images of a dog with portosystemic shunt.

breed (14). To the authors' knowledge, measurement of SBA concentration for PSS prognosis evaluation in Maltese dogs has not been yet investigated. In order to determine whether SBA can be used to assess the surgical prognosis of PSS in Maltese, the present study evaluated pre- and post-operative serum biochemistry profiles including SBA concentrations in Maltese and other breeds of dogs with PSS.

Materials and Methods

Inclusion criteria. Medical records of Maltese dogs without PSS and Maltese dogs or other breeds of dogs with congenital PSS that underwent surgical attenuation of the shunt at the Veterinary Teaching Hospital in Cheongju, Korea, between 2018 and 2020 were retrospectively reviewed. Since the prognosis might differ depending on the shunt type (6), laboratory data of Maltese and other breed dogs with portocaval shunt were compared. Dogs received medications that could affect results of blood tests were excluded from this study.

Preoperative evaluation. Data included breed, age, sex, body weight, shunt type, and results of laboratory tests. Serum biochemistry profiles included alanine aminotransferase (ALT) activity, alkaline phosphatase (ALP) activity and concentrations of albumin, ammonia, SBA, and blood urea nitrogen (BUN). Blood tests were performed pre- and post-operatively. Short-term follow-up was conducted within a month after surgery. Dogs with follow-up periods of more than 6 months were defined as having a long-term follow-up.

Imaging. CT images of each dog were taken using a four-row multi-detector CT scanner (HiSpeed QX/i; GE Medical Systems, Milwaukee, WI, USA). A CT angiography was performed following previous literature (Figure 1A and B) (15). Shunt types were

classified according to the insertion site (portocaval, portophrenic, and portoazygos shunt) (6). Data were analyzed using a digital image measurement program (eFilm Workstation 4.1; Merge Healthcare, Hartland, WI, USA).

Surgical procedure. Animals were pre-medicated with midazolam (0.2 mg/kg, IV) and butorphanol (0.2 mg/kg, IV). Anesthesia was induced with propofol (6 mg/kg, IV) and maintained by isoflurane. After anesthetic stabilization, a ventral midline celiotomy was performed and the shunt was visualized. After dissection of the perivascular fascia, the decision to use ARC or cellophane band was made based on the surgeon's preference. The ARC of 3.5 or 5 mm in diameter was used and placed as previously recommended (16). When using a cellophane band, a strip of the cellophane band (12 mm in width) was folded in triple layers (4 mm in final width) (17). It was placed around the shunt and secured using surgical clips. Peri- and post-operative pain were managed by butorphanol or fentanyl transdermal patch (2 µg/kg/h).

Statistical analysis. Data between two groups were analyzed by Mann-Whitney *U*-test. All statistical analyses were performed using GraphPad Prism version 6.01 for Windows and a *p*-value <0.05 was considered significant. Data are expressed as mean±standard deviation.

Results

Demographics. A total of 23 dogs were reviewed. Breeds included Maltese (n=10), Pomeranian (n=3), Bichon Frise (n=3), Italian Greyhound (n=2), Poodle (n=1), White Terrier (n=1), and mixed (n=3). No significant differences were observed in age or body weight between Maltese and other breeds of dogs. Among Maltese dogs, the portocaval shunt was identified in 8 dogs. The portophrenic and portoazygos

Table I. *Demographics of Maltese and non-Maltese dogs with portosystemic shunt.*

Variables	Maltese	Non-Maltese
Sex (n)		
Sexually intact males	1	1
Castrated males	8	5
Sexually intact females	1	6
Spayed females		1
Age (months)		
Mean±SD	27±23	26±17
Median	14	24
Range	9-74	8-62
Body weight (kg)		
Mean±SD	3.3±1.5	4.1±1.1
Median	3.0	4.3
Range	1.5-6.3	1.7-5.4
Shunt type (n)		
Portocaval shunt	8	9
Portophrenic shunt	1	3
Portoazygos shunt	1	1

SD: Standard deviation.

shunts were identified in one dog each. Depending on types of shunts in other breeds of dogs, portocaval shunt (n=9) was the most common, followed by portophrenic shunt (n=3) and portoazygos shunt (n=1) (Table I). Subsequent laboratory results were conducted for dogs with portocaval shunt (8 Maltese dogs and 9 non-Maltese dogs, respectively).

Serum bile acid concentrations in Maltese dogs without PSS. Medical records of 30 Maltese dogs without PSS were reviewed. Maltese dogs without PSS were significantly older than Maltese dogs with PSS in this study. There was no significant difference in body weight between the two groups. According to SBA concentration in the present study, 25 out of 30 Maltese dogs without PSS showed SBA levels within the RI (Table II).

Preoperative evaluation. Both Maltese and non-Maltese dogs with portocaval shunt showed ALT, ALP, and SBA levels above RIs. Preoperative ALP and SBA levels were significantly higher in Maltese dogs than in non-Maltese dogs. There was no significant difference in albumin, ALT, ammonia, or BUN level between the two groups.

Short-term clinical outcomes (within a month). Follow-up blood tests were mainly performed at two weeks after surgery. Both Maltese and non-Maltese dogs showed significantly lower ammonia and SBA levels than preoperative values. ALT and ALP activities were significantly decreased in Maltese dogs (Table III). In non-Maltese dogs, BUN levels were significantly increased (Table IV). During the short-term follow-up, no

Table II. *Demographics and serum bile acid concentrations of Maltese dogs without portosystemic shunt (PSS).*

Variables	Maltese dogs without PSS
Sex (n)	
Sexually intact males	3
Castrated males	12
Sexually intact females	3
Spayed females	12
Age (months)	
Mean±SD	94±48
Median	106
Range	8-176
Body weight (kg)	
Mean±SD	3.3±1.1
Median	3.2
Range	1.6-6.4
Bile acid (μmol/l)	
Mean±SD	8±12
Median	0
Range	0-35
Reference interval	0-25

SD: Standard deviation.

Table III. *Comparison of pre- and post-operative serum biochemistry in Maltese dogs with portocaval shunt.*

Measurement	Pre-OP	Post-OP	RI
Albumin (g/dl)	2.7±0.4	2.9±0.3	2.6-3.3
ALT (IU/l)	196±117	74±73*	21-102
ALP (IU/l)	888±319	517±135*	29-97
Bile acid (μmol/l)	192±53	36±45*	0-25
Ammonia (μmol/l)	51±28	6±4*	0-98
BUN (mg/dl)	8.2±3.3	13.6±4.8	7-25

Values expressed as Mean±SD. **p*<0.05 compared to Pre-OP group. OP: Operative; RI: reference interval; ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; SD: standard deviation.

Table IV. *Comparison of pre- and post-operative serum biochemistry in non-Maltese dogs with portocaval shunt.*

Measurement	Pre-OP	Post-OP	RI
Albumin (g/dl)	2.6±0.5	3.0±0.5	2.6-3.3
ALT (IU/l)	132±133	73±30	21-102
ALP (IU/l)	500±255	599±154	29-97
Bile acid (μmol/l)	137±36	19±21*	0-25
Ammonia (μmol/l)	63±39	8±7*	0-98
BUN (mg/dl)	6.5±1.6	10.4±3.6*	7-25

Values expressed as Mean±SD. **p*<0.05 compared to Pre-OP group. OP: Operative; RI: reference interval; ALT: alanine aminotransferase; ALP: alkaline phosphatase; BUN: blood urea nitrogen; SD: standard deviation.

significant difference was identified in serum biochemistry profiles between the two groups.

Long-term clinical outcomes (more than 6 months). Long-term follow-up was available for 2 Maltese dogs and 3 non-Maltese dogs. Serum biochemistry profiles including SBA concentrations in both groups were within RI. ALP activities were above RI. The mean ALP was 269 IU/l (RI, 29-97 IU/l) in Maltese dogs and 308 IU/l in non-Maltese dogs.

Discussion

A previous study documented female over-representation of PSS in Maltese (11 out of 15 dogs) (18). However, another study reported a similar ratio between sexes (8 females and 11 males) (14). The present study revealed that male Maltese dogs were predisposed to PSS (9 out of 10 dogs). However, as numbers of dogs evaluated in previous and present studies were small, it was difficult to describe whether distribution of PSS in Maltese had a difference according to sex. When shunt types were evaluated according to the site of insertion, a shunt that was inserted into the vena cava was the most prevalent in both Maltese and other breeds of dogs, similar to previous literatures (6, 17). Surgical attenuation of a portocaval shunt was conducted using ARC or cellophane band. As both ARC and cellophane band have already been verified through various studies (10, 16, 17, 19, 20), these two methods were used according to the surgeon's preference. Although cellophane band was applied in only 3 out of 17 dogs in the present study, both methods were effective considering resolution of preoperative clinical signs and postoperative normalization of serum biochemistry profiles of dogs. Between serum biochemistry profiles in evaluating pre- and post-operative prognosis of dogs with PSS, previous studies have suggested not to use SBA concentration for diagnosis of PSS in Maltese dogs as high levels can be seen in normal dogs of this breed (13, 14). However, the authors also mentioned that these investigations might result in not using SBA concentration as a routine test for diagnosis and monitoring the response to surgery of PSS. In addition, diagnosis between normal and PSS Maltese dogs mainly relied on ammonia tolerance test and/or visual confirmation of the shunt in previous studies (13, 14). Among various liver diseases, portal vein hypoplasia may reveal similar clinical presentation and laboratory finding, although those are generally less pronounced than those in PSS (21). Furthermore, the ammonia tolerance test can also give false-negative results for portal vein hypoplasia or residual shunting (21, 22). Recently, it has been reported that such hepatic disorders might not be revealed through laboratory testing alone. However, these hepatic disorders can be diagnosed when laboratory testing is combined with other diagnostic methods such as scintigraphy or CT angiography (21, 23). Unlike results of previous studies

(13, 14), SBA concentrations in Maltese dogs without PSS were generally within RI in the present study.

Taken together, it is presumed that Maltese dogs with portal vein hypoplasia might have been included in normal groups at that time. Consequently, although it is not recommended to diagnose PSS based only on SBA levels (12, 13, 24), evaluating the prevalence and surgical prognosis of PSS through SBA concentration combined with other serum biochemistry factors is useful in Maltese dogs.

Funding

This research was supported by the Chungbuk National University Korea National University Development Project (2022).

Conflicts of Interest

The Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

DK, DP, K-JN and GK designed the study. DK, HA and BA analyzed the data. The manuscript was written by DK, HO and GK. All Authors critically revised the manuscript and approved the final version.

References

- Papamichail M, Pizani M and Heaton N: Congenital portosystemic venous shunt. *Eur J Pediatr* 177(3): 285-294, 2018. PMID: 29243189. DOI: 10.1007/s00431-017-3058-x
- Kim MJ, Ko JS, Seo JK, Yang HR, Chang JY, Kim GB, Cheon JE and Kim WS: Clinical features of congenital portosystemic shunt in children. *Eur J Pediatr* 171(2): 395-400, 2012. PMID: 21912894. DOI: 10.1007/s00431-011-1564-9
- Berent AC and Tobias KM: Portosystemic vascular anomalies. *Vet Clin North Am Small Anim Pract* 39(3): 513-541, 2009. PMID: 19524792. DOI: 10.1016/j.cvsm.2009.02.004
- Winkler JT, Bohling MW, Tillson DM, Wright JC and Ballagas AJ: Portosystemic shunts: diagnosis, prognosis, and treatment of 64 cases (1993-2001). *J Am Anim Hosp Assoc* 39(2): 169-185, 2003. PMID: 12617545. DOI: 10.5326/0390169
- Tobias KM and Rohrbach BW: Association of breed with the diagnosis of congenital portosystemic shunts in dogs: 2,400 cases (1980-2002). *J Am Vet Med Assoc* 223(11): 1636-1639, 2003. PMID: 14664452. DOI: 10.2460/javma.2003.223.1636
- Kraun MB, Nelson LL, Hauptman JG and Nelson NC: Analysis of the relationship of extrahepatic portosystemic shunt morphology with clinical variables in dogs: 53 cases (2009-2012). *J Am Vet Med Assoc* 245(5): 540-549, 2014. PMID: 25148096. DOI: 10.2460/javma.245.5.540
- Greenhalgh SN, Dunning MD, McKinley TJ, Goodfellow MR, Kelman KR, Freitag T, O'Neill EJ, Hall EJ, Watson PJ and Jeffery ND: Comparison of survival after surgical or medical treatment in dogs with a congenital portosystemic shunt. *J Am Vet Med Assoc* 236(11): 1215-1220, 2010. PMID: 20513200. DOI: 10.2460/javma.236.11.1215

- 8 Taboada J and Dimski DS: Hepatic encephalopathy: clinical signs, pathogenesis, and treatment. *Vet Clin North Am Small Anim Pract* 25(2): 337-355, 1995. PMID: 7785167.
- 9 Mehl ML, Kyles AE, Case JB, Kass PH, Zwingenberger A and Gregory CR: Surgical management of left-divisional intrahepatic portosystemic shunts: outcome after partial ligation of, or ameroid ring constrictor placement on, the left hepatic vein in twenty-eight dogs (1995-2005). *Vet Surg* 36(1): 21-30, 2007. PMID: 17214816. DOI: 10.1111/j.1532-950X.2007.00231.x
- 10 Traverson M, Lussier B, Huneault L and Gatineau M: Comparative outcomes between ameroid ring constrictor and cellophane banding for treatment of single congenital extrahepatic portosystemic shunts in 49 dogs (1998-2012). *Vet Surg* 47(2): 179-187, 2018. PMID: 29247521. DOI: 10.1111/vsu.12747
- 11 Bristow P, Tivers M, Packer R, Brockman D, Ortiz V, Newson K and Lipscomb V: Long-term serum bile acid concentrations in 51 dogs after complete extrahepatic congenital portosystemic shunt ligation. *J Small Anim Pract* 58(8): 454-460, 2017. PMID: 28660694. DOI: 10.1111/jsap.12685
- 12 Gerritzen-Bruning MJ, van den Ingh TS and Rothuizen J: Diagnostic value of fasting plasma ammonia and bile acid concentrations in the identification of portosystemic shunting in dogs. *J Vet Intern Med* 20(1): 13-19, 2006. PMID: 16496918. DOI: 10.1892/0891-6640(2006)20[13:dvoftp]2.0.co;2
- 13 Tisdall PL, Hunt GB, Tsoukalas G and Malik R: Post-prandial serum bile acid concentrations and ammonia tolerance in Maltese dogs with and without hepatic vascular anomalies. *Aust Vet J* 72(4): 121-126, 1995. PMID: 7646375. DOI: 10.1111/j.1751-0813.1995.tb15029.x
- 14 O'Leary CA, Parslow A, Malik R, Hunt GB, Hurford RI, Tisdall PL and Duffy DL: The inheritance of extra-hepatic portosystemic shunts and elevated bile acid concentrations in Maltese dogs. *J Small Anim Pract* 55(1): 14-21, 2014. PMID: 24299127. DOI: 10.1111/jsap.12156
- 15 Stieger SM, Zwingenberger A, Pollard RE, Kyles AE and Wisner ER: Hepatic volume estimation using quantitative computed tomography in dogs with portosystemic shunts. *Vet Radiol Ultrasound* 48(5): 409-413, 2007. PMID: 17899972. DOI: 10.1111/j.1740-8261.2007.00268.x
- 16 Vogt JC, Krahwinkel DJ Jr, Bright RM, Daniel GB, Toal RL and Rohrbach B: Gradual occlusion of extrahepatic portosystemic shunts in dogs and cats using the ameroid constrictor. *Vet Surg* 25(6): 495-502, 1996. PMID: 8923729. DOI: 10.1111/j.1532-950X.1996.tb01449.x
- 17 Hunt GB, Kummeling A, Tisdall PL, Marchevsky AM, Liptak JM, Youmans KR, Goldsmit SE and Beck JA: Outcomes of cellophane banding for congenital portosystemic shunts in 106 dogs and 5 cats. *Vet Surg* 33(1): 25-31, 2004. PMID: 14687183. DOI: 10.1111/j.1532-950X.2004.04011.x
- 18 Van den Bossche L, van Steenbeek FG, Favier RP, Kummeling A, Leegwater PA and Rothuizen J: Distribution of extrahepatic congenital portosystemic shunt morphology in predisposed dog breeds. *BMC Vet Res* 8: 112, 2012. PMID: 22784395. DOI: 10.1186/1746-6148-8-112
- 19 Youmans KR and Hunt GB: Experimental evaluation of four methods of progressive venous attenuation in dogs. *Vet Surg* 28(1): 38-47, 1999. PMID: 10025639. DOI: 10.1053/jvet.1999.0038
- 20 Youmans KR and Hunt GB: Cellophane banding for the gradual attenuation of single extrahepatic portosystemic shunts in eleven dogs. *Aust Vet J* 76(8): 531-537, 1998. PMID: 9741718. DOI: 10.1111/j.1751-0813.1998.tb10208.x
- 21 Devriendt N, Or M, Paepe D, Vandermeulen E, Hesta M, De Cock HEV and de Rooster H: Portal vein hypoplasia in dogs. *Vlaams Diergeneesk Tijdschr* 83(5): 234-239, 2014. DOI: 10.21825/vdt.v83i5.16635
- 22 Devriendt N, Serrano G, Paepe D and de Rooster H: Liver function tests in dogs with congenital portosystemic shunts and their potential to determine persistent shunting after surgical attenuation. *Vet J* 261: 105478, 2020. PMID: 32741493. DOI: 10.1016/j.tvjl.2020.105478
- 23 von Stade LE, Shropshire SB, Rao S, Twedt D and Marolf AJ: Prevalence of portal vein thrombosis detected by computed tomography angiography in dogs. *J Small Anim Pract* 62(7): 562-569, 2021. PMID: 33687080. DOI: 10.1111/jsap.13315
- 24 Kerr MG and van Doorn T: Mass screening of Irish wolfhound puppies for portosystemic shunts by the dynamic bile acid test. *Vet Rec* 144(25): 693-696, 1999. PMID: 10420483. DOI: 10.1136/vr.144.25.693

Received January 9, 2023

Revised January 25, 2023

Accepted February 3, 2023