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**KARYA ILMIAH : JURNAL ILMIAH**

Judul Jurnal Ilmiah (Artikel) : Cerebrospinal fluid contents and risk of shunt exposure in hydrocephalus  
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 g. Terindex : Sinta (S2)

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Struktur artikel lengkap sesuai dengan author guidelines. State of art dapat mengarahkan ke manfaat riset ini. Namun terdapat istilah CSF parameter pada tujuan penelitian (abstract) namun di manuscript istilah yang digunakan CSF contents (seperti dalam judul). Istilah shunt exposure yang menjadi topic utama juga tidak dijelaskan pada background literature.

**2. Ruang lingkup dan kedalaman pembahasan:**

Merupakan penelitian retrospective yang melibatkan 513 kasus VP shunt. Diskusi lebih banyak mengutarakan background literature yang seharusnya ada diIntroduction. Banyak menceritakan komplikasi post shunting tapi lebih ke migration, infection and failure (functional). Apakah sama antara exposure dengan migration? Pembaca akan kesulitan memahani.

**3. Kecukupan dan kemutakhiran data/informasi dan metodologi:**

Metode penelitian dijelaskan, namun kriteria inklusi/ eksklusi tidak dijelaskan begitu juga dengan definisi operasional/ kriteria shunt exposure. Hal ini sangat mengganggu karena pada background literature tidak dijelaskan definisinya. CSF contents, apakah hanya PMNs, protein dan glucose? Bila menggunakan 3 kriteria berdasarkan penelitian siapa? Tidak dijelaskan apakah ada kriteria eksklusi pada pasien dengan diagnosis hydrocephalus post infeksi selaput otak yang secara teori mempunyai resiko lebih besar terjadi shunt exposure

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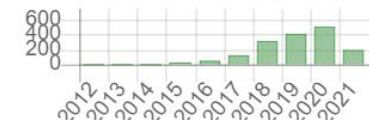
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# The characteristics of neurocognitive function in farmers exposed to chronic pesticides at Banjar Tengah Kelod, Kerambitan, Tabanan, Bali, Indonesia



Dewa Putu Gde Purwa Samatra<sup>1\*</sup>, Ni Luh Putu Dirasandhi Semedi Putri<sup>1</sup>

## ABSTRACT

**Purpose:** This study aims to evaluate the characteristics of neurocognitive function in farmers exposed to chronic pesticides.

**Material and Methods:** This study uses a descriptive cross-sectional design with total sampling methods. The study was conducted from 1<sup>st</sup> January 2019 until 31<sup>st</sup> January 2019 located in Banjar Tengah Kelod, Kerambitan sub-district, Tabanan district, Bali, Indonesia.

**Results:** A total of 60 samples, consisted of 36 samples (60%) were women and 24 samples (40%) were men were obtained. The median age of the study sample was 55 year-old. Most of the samples who experienced neurocognitive impairment used organophosphate pesticides (60%), followed by organochlorine (20%), carbamate (13.3%), and pyrethroid (6.7%). Organophosphate users experienced neurocognitive impairment in both memory domain

(mean score of 1.5 what scoring was used?) and visuospatial executive functions (mean score of 1, what scoring system?). The mean memory function score in the organochlorine user group was the highest compared to other groups of pesticide users while the average score of visuospatial function was 1. The samples of the study using carbamate pesticides had the same average score in both domains of neurocognitive function. The mean score of memory function in pyrethroid user was 2.5 and the average score of executive visuospatial function was 1.

**Conclusion:** Chronic exposure to the four types of pesticides provided a picture of neurocognitive function impairment, including memory, visuospatial and executive functions. This result did not show clinical significance. The addition of sample size and analytic method studies should be considered for further research.

**Keywords:** neurocognitive, pesticides, farmers

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## INTRODUCTION

Neurocognitive function is a conscious mental activity, such as thinking, remembering, learning, and using language. Neurocognitive function is influenced by several factors, such as biological, socio-economic, and environmental.<sup>1</sup> One of the much debated environmental factors of concern is the use of pesticides.

Pesticides are all substances or mixtures of chemical or biological substances that aim to repel, kill, and control pests, and regulate plant growth.<sup>2</sup> The chemical structure of pesticides is divided into four main groups, namely: organophosphate, carbamate, organochlorine, and pyrethrin and pyrethroids. Pesticides have been used extensively in agriculture. Agricultural improvement correlates with increased use of pesticides. Bali is one of the provinces with an increasing agricultural yield.<sup>3</sup>

The pathophysiology of pesticide exposure causes cognitive function impairment is still being debated. A study conducted by Luo and Chen

shows that administration of pesticides containing deltamethrin and carbofuran to mice once a day for 28 days showed a decrease in spatial memory function. A meta-analysis study of 1256 articles by Munoz-Quezada *et al.* also concluded that there was association between chronic exposure of organophosphates pesticides with decreased neurocognitive function in exposed workers.<sup>4</sup> Other studies have been conducted on 191 cases with a history of organophosphate pesticide sprayers, namely chlorpyrifos for a minimum of 2 years compared with 189 control group who was never exposed. However, the results of examination of visuospatial, psychomotor, and neurocognitive functions in these two groups did not differ significantly.<sup>5</sup>

Factors that encouraged researchers to do this research are the high use of pesticides in Bali, the theory of neurocognitive function impairment related to long-term use of pesticides which is still controversial, the risk of decreasing quality of life that can be experienced related to neurocognitive

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# The effect of tomato juice on the expression of matrix metalloproteinase-2 (MMP-2) and type-1 collagen on the vaginal wall of the menopausal rats



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## ABSTRACT

**Background:** Aging is a multifactorial phenomenon that is characterized by a decrease in physiological functions that increases with age. Free radicals cause oxidative stress, which plays a role in the aging process. The accumulation of reactive oxygen compounds increases matrix metalloproteinase-2. Collagen can be directly destroyed by reactive oxygen compounds or through the induction of MMPs. Tomato fruit is an antioxidant, which acts as a binder and damper of free radicals that activate collagen damage. This study aims to assess the effect of tomato juice on the expression of MMP-2 and type-1 collagen on the vaginal wall of the menopausal rat.

**Methods:** This was a true experimental study, using Sprague-Dawley rats and tomato juice (*Solanum lycopersicum*). Expression of MMP-2 and type-1 collagen was examined using immunohistochemistry staining. Twenty-four healthy female rats, aged 4 months weighing 150-200 grams, were divided into 4 groups, each group as many as 6 rats. The negative control group (NC) was a group of rats with a sham procedure, given aquades for 28 days. The positive control group (PC) was bilaterally ovariectomized rats, given aquades for 28 days. The first treatment group (P1) was bilaterally ovariectomized rats, given tomato juice with a dose of 11 g / 200 g BW / day. The second treatment group (P2) was bilaterally ovariectomized rats, given tomato juice with a dose of 15 g / 200 g BW / day. Data

analysis used the One-way ANOVA statistical test ( $\alpha = 0.05$ ) and different tests between groups using Games-Howell and Tukey HSD. The association between tomato juice and the expression of MMP-2 and type-1 collagen used regression tests.

**Results:** This study found that the lowest expression of MMP-2 was NC group ( $2.07 \pm 0.84$ ), and the highest was the PC group ( $5.72 \pm 1.91$ ). The mean MMP-2 expression in the treatment groups was lower than the PC group but still higher than the NC group. There was a significant difference in MMP-2 expression between groups ( $p = 0.000$ ). There was a negative correlation between tomato juice administration and MMP-2 expression ( $b = -0.592$ ). The lowest type-1 collagen expression was PC group ( $3.83 \pm 1.44$ ), and the highest was the P2 group ( $7.27 \pm 2.21$ ). The mean type-1 collagen expression in the treatment groups was higher than the PC group. There were significant differences of type-1 collagen expression between groups ( $p = 0.012$ ). There was a positive correlation between tomato juice administration and type-1 collagen expression ( $b = 0.682$ ).

**Conclusions:** Tomato juice administration can reduce the expression of MMP-2 and increase the expression of type-1 collagen on the vaginal wall of the menopausal rat. The higher the dose of tomato juice, the higher the expression of type-1 collagen.

**Keywords:** MMP-2, menopause, tomato juice, type-1 collagen

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## INTRODUCTION

Menopause is a period of life that is passed by all women who have a long life. Improved welfare and better economic standards bring a higher life expectancy for women.<sup>1</sup> Aging is a multifactorial phenomenon that is characterized by a decrease in physiological functions that increases with age. This decrease in function is also associated with the accumulation of damage to the metabolic pathway. The aging process is expressed in various theories, and the most popular is the theory of free radicals.<sup>2</sup> Free radicals are chemical compounds in the form of atoms or molecules that have unpaired electrons in the outer layer. These chemical compounds have

one or more free electrons so that in large quantities can cause oxidative stress. Oxidative stress occurs because of an imbalance between oxidants and antioxidants, which then has the potential to cause cell damage. Damage to these important molecules plays a role in degenerative changes in the aging process.<sup>3,4,5</sup>

Normal conditions, free radicals can be muted by the body, because naturally, the body produces antioxidants, such as catalase and superoxide dismutase. Antioxidants functions to prevent the growth of free radicals in the body, by donating one or more electrons to free radicals so that free radicals that were originally very reactive become stable.<sup>6,7</sup>

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# Cerebrospinal fluid contents and risk of shunt exposure in hydrocephalus



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## ABSTRACT

**Background:** Exposure of the shunt is a rare but severe complication after ventriculoperitoneal (VP) shunt placement. It is unclear whether particular levels of cerebrospinal fluids (CSF) protein, glucose, or polymorphonuclears (PMNs) may influence the shunt exposure in high-risk individuals.

This study aims to find the relation between CSF parameters and shunt exposure.

**Methods:** Examined preoperative CSF characteristics included CSF colour, protein, glucose, and PMNs content in 513 patients with

hydrocephalus. Mann-Whitney test was used to determine the correlation between CSF parameters and shunt exposure.

**Results:** Shunt exposure was detected in 25 cases (4.87%). There was a significant relationship between distal tip exposure with preoperative glucose ( $p=0.000$ ), protein level ( $p=0.007$ ), or PMNs count ( $p=0.043$ ).

**Conclusion:** Preoperative CSF contents had a significant correlation with shunt exposure in hydrocephalus patients.

**Keywords:** glucose; protein; polymorphonuclear cells; cerebrospinal fluid; shunt exposure

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## INTRODUCTION

Cerebrospinal fluid (CSF) diversion by ventriculoperitoneal (VP) shunt installation is the backbone of hydrocephalus management in pediatric as well as in adult patients. Despite this, VP shunting is still susceptible to some failures. The most common cause of shunt revisions remains to be VP shunt malfunction including obstruction, infection, over drainage, subdural hematoma, and catheter migration.<sup>1,2,10,15</sup>

Exposure of the shunt is a rare but serious complication after VP shunt placement. The site of migration has been reported to be in various hollow organs including small, large intestine and stomach. More rarely, protrusion of catheter's distal tip to rectum, mouth, vagina and fallopian tubes, bladder, and scrotum has been documented.<sup>3-5</sup> The pathophysiology of catheter migration has not been completely understood, with increased intra-abdominal pressure, abdominal wall contraction, malnutrition, poor host condition, weak bowel movement, type of catheter, and shunt insertion procedure considered as potential risk factors.<sup>6,11,18</sup>

It is unclear whether particular levels of protein, glucose, or polymorphonuclear cells (PMNs) in the CSF can influence the shunt exposure in high-risk individuals.<sup>7-9</sup> As the investigation of this matter has not been thoroughly studied, therefore, we conducted this research to investigate whether there

is an association between the CSF contents and shunt exposure in hydrocephalus patients in our centre at Kariadi General Hospital, Semarang, Indonesia.

## METHODS

We conducted an observational retrospective study to assess the correlation between CSF contents with shunt exposure. Five hundred and thirteen VP shunt installation surgeries performed in our neurosurgical centre in Semarang, Indonesia, from 2010 to 2015. This study has been reviewed and approved by the Ethical Committee of Kariadi General Hospital, Semarang, Indonesia.

We evaluated preoperative CSF analysis performed for each surgery. We compared the level of protein, glucose, and PMNs count between the exposed group and the non-exposed group. Exposure group was defined as the exposure of distal tip of the catheter outside the peritoneal chamber. We recorded the demographic profiles and CSF characteristics in patients with and without shunt migration. Data analysis was performed with SPSS Statistics 19 (IBM, USA). Descriptive data, including sex, age, and CSF colour, were described for each group. We used the Mann-Whitney test to determine the significance between CSF parameters and VP shunt exposure. A significant correlation was determined if  $p < 0.05$ .

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## RESULTS

We performed 513 cases of VP shunt installation in our centre in Semarang, Indonesia from 2011 to 2015. The average age at surgery was  $13.63 \pm 18.67$  years ranged from 5 days old to 52 years old, consisted of 295 (54.8%) male and 243 (45.2%) female patients. The exposed shunt was observed in 25 patients (4.87%) in 15 male and ten female patients respectively, which were divided into retroauricular exposure in 10 cases (40.0%), anal orifice exposure in 10 cases (40.0%), and abdominal wall

exposure in 5 cases (20.0%). Patients' demography and CSF characteristics are presented in Table 1.

We found significant relationships between preoperative CSF contents with shunt exposure incidence. Both protein ( $p=0.007$ ) and PMNs ( $p=0.043$ ) count was higher in the exposed group compared to the non-exposed group, while the glucose contents were lower ( $p=0.000$ ). In the exposed group, the amount of PMNs in CSF was increased on 15 cases, normal on 7 cases, and decreased in 3 cases. The protein level was higher than 150 mg/dL on 23 cases and normal in 2 cases. The glucose level was increased on 3 cases, normal in 8 cases, and decreased in 14 cases (Table 2).

**Table 1** Patients demography and CSF characteristics

	<i>n</i> (%); Mean $\pm$ SD	Group	
		Malfunctioning ( <i>n</i> =25)	Non- malfunctioning ( <i>n</i> =513)
<b>Sex</b>			
Male	295 (54.8)	15 (5.1)	280 (94.9)
Female	243 (45.2)	10 (4.1)	233 (95.9)
<b>Age</b>	$13.63 \pm 18.67$	$5.33 \pm 11.03$	$15.04 \pm 18.88$
<b>CSF Color</b>			
Slightly turbid	2 (0.4)	2 (100.0)	0 (0.0)
Brownish red	2 (0.4)	0 (0.0)	2 (100.0)
Clear	380 (70.6)	13 (3.4)	367 (96.6)
Turbid	15 (2.8)	0 (0.0)	15 (100.0)
Yellow	28 (5.2)	0 (0.0)	28 (100.0)
Slightly turbid yellow	4 (0.7)	1 (25.0)	3 (75.0)
Clear yellow	60 (11.2)	3 (5.0)	57 (95.0)
Turbid yellow	17 (3.2)	1 (5.9)	16 (94.1)
Light yellow	7 (1.3)	4 (57.1)	3 (42.9)
Red	15 (2.8)	0 (0.0)	15 (2.9)
Turbid red	1 (0.2)	0 (0.0)	1 (100.0)
Pink	7 (1.3)	1 (14.3)	6 (85.7)
<b>Exposed location</b>			
Retroauricula	10 (40.0)	10 (100.0)	0 (0.0)
Abdomen	5 (20.0)	5 (100.0)	0 (0.0)
Anus	10 (40.0)	10 (100.0)	0 (0.0)

CSF = cerebrospinal fluid; SD = standart deviation

**Table 2** Comparison of CSF contents between groups

	Mean count (Range)			<i>P</i>
	Malfunctioning ( <i>n</i> = 25)	Non- malfunctioning ( <i>n</i> = 513)	Normal Range	
Protein	177.5 (0.63 – 727.5)	56.5 (0.3 – 797.1)	15 – 45	0.007
Glucose	49 (2 – 90)	59 (0 – 566)	45 – 80	0.043
PMN	12 (0 – 245)	2 (0 – 293)		0.000

PMN = polymorphonuclear cells; Normal range for protein is measured in mg/dL, glucose in mg/dL, PMN in cell/mm<sup>3</sup>

## DISCUSSION

Cerebrospinal fluid flow alteration with VP shunt placement has been the pillar of treatment in both adult and pediatric hydrocephalus. However, this procedure is associated with postoperative complication, including mechanical failure, infection, and functional defects.<sup>7,12</sup> Mechanical failure consists of equipment failure, breakage, obstruction, and migration of either proximal or distal catheter tip.

One of the rare complications of VP shunt installation is the migration of the distal catheter leading to distal tip exposure. Several authors have reported the site of shunt exposure including small and large intestine, stomach, rectum, mouth, vagina and fallopian tubes, bladder, breast, and scrotum, although the prevalence was relatively low (0.01%–1.4%).<sup>(5,13,18)</sup> Our observation-only recorded three sites of exposure in 25 patients, which were retroauricular (40.0%), abdominal wall (40.0%), and anal orifice (20.0%).

Several mechanisms have been suggested to explain the pathogenesis of shunt exposure, including foreign body reaction, localised infection, and local anatomic disadvantage. One of the hypotheses regarding the shunt exposure is the localised infections around the shunt materials, which subsequently create abscess and skin fistula leading to the exposure of shunt's tip outside the skin.<sup>2,6,8</sup> Other explanation is that the continuous stress on the skin may induce localised ischemia and necrosis later, forming an exit port for catheter, especially in susceptible regions with the thinner skin surface and weaker muscle contraction.<sup>9,14,17</sup> The anatomic site differences may explain the different cause of exposure, such as the thinning of the skin because of increased head circumference for retroauricular exposure, increased intra-abdominal pressure and weaker abdominal muscle in abdominal wall exposure, or peristaltic force expulsion leading to anal orifice exposure.

Assumed risk factors for shunt migration, including increased intra-abdominal pressure,



abdominal wall contraction, malnutrition, poor host condition, obesity, weak bowel movement, type of catheter, and shunt insertion procedure.<sup>3,13,14</sup> Besides these established factors, we found that preoperative CSF contents had a significant relationship with shunt exposure in hydrocephalus patients. Our results demonstrated that higher PMNs and protein and lower glucose content were related to shunt exposure, suggesting that preoperative infection of the CSF spaces might contribute to the occurrence of later exposure. The microorganism might spread via the shunt or during surgical insertion, leading to localised infection and subsequent exposure.<sup>16,17</sup>

We also observed that shunt exposure affected younger patients ( $5.33 \pm 11.03$  years in the exposure group versus  $15.04 \pm 18.88$  years in the non-exposure group). Although shunt complication is more common in pediatric patients because of their relatively thinner scalp compared to adults and weaker immune system, we also observed a case of shunt exposure in the abdominal wall on a 52-year-old man.

The limitation of this study included the lack of data regarding the cause of hydrocephalus, nutritional status as malnutrition might lead to poor immunity and propensity to infection, and the type of shunt implanted on each patient in the medical records. We also did not obtain a complete evaluation of the responsible microorganism, causing the infection of the shunt system. A further and more detailed study in the future will bring a better understanding of the factors attributed to VP shunt exposure.

## CONCLUSION

Our findings demonstrated that preoperative CSF contents had a significant correlation with shunt exposure in hydrocephalus patients. Higher PMNs and protein and lower glucose content were related to shunt exposure. Consequently, it is imperative to determine the timing of shunt insertion based on CSF characteristics. Such information must be taken into account when neurosurgeons are executing and modifying shunt networks in individuals with altered CSF states.

## CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding publication of current study.

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