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ANALYSIS OF PREDICTOR INDEX OF DETERMINANT FACTORS OF DIABETIC NEUROPATHY PAIN ON THE EFFECTIVENESS OF LOCAL ANESTHESIA LIDOCAINE INJECTION THERAPY LIDOCAINE FOR DIABETIC NEUROPATHIC PAIN

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Abstract

Background: Diabetic neuropathy is a common complication of diabetes mellitus that requires relatively long-term management. Health status is determined by genetic factors, behavioral factors, environmental factors, and healthcare service factors. These factors are also associated with determinants of disease, including neuropathic pain in diabetes mellitus.

Materials and Method: This study involved 244 diabetic neuropathic pain patients who received lidocaine injections at the Bhayangkara Hospital Pusdik Brimob Watukosek from August 2020 to April 2021. Sampling was carried out using the consecutive sampling method based on medical records at the peak of visits to the pain clinic. The design of this study was observational analytic with a cross-sectional approach.

Results: Genetic factors that showed significant results were the age category (0.047) and family history (0.004). In behavioral factors, significant results were found in the categories of physical activity (0.010), education level (0.001), and smoking (<0.001). In terms of health services, significant results were found in the category of regularity of treatment (<0.001), for environmental factors, significant results were found in the category of alternative therapy (0.001) and for quality of life with SCREEM (0.036).

Conclusion: The results of the logistic regression analysis, the influencing factors are in accordance with HL Blum's concept regarding the effectiveness of using lidocaine local anesthetic therapy by 50%.

Keywords: Diabetes Mellitus, Diabetic Neuropathic Pain, Lidocain, Medicine.

INTRODUCTION

Prevalence of diabetes mellitus in Indonesia at the age of ≥15 years by 2% in 2018, up from the previous data in 2013 of 1.5%. Based on a study of 100.0% of patients with peripheral diabetic neuropathy in Korea (n = 1338), 43.1% (577 patients) experienced diabetic neuropathic pain (Won et al., 2014). In addition, there were 71.90% (691 patients) who experienced chronic complications of neuropathy in patients with diabetes mellitus in the internal medicine polyclinic of Dr. M. Soewandi Hospital in 2016. 497 of them were patients with type 2 diabetes mellitus. Around 20-30% of patients with type 2 diabetes mellitus experience neuropathic pain (Rahmawati & Hargono, 2018).

Diabetic neuropathy is a common complication of diabetes mellitus that requires relatively long treatment. Thus, it can interfere with and reduce the quality of life (utility) of sufferers, obstacles that occur due to the pain they suffer such as the ability to work, mobility, and social impacts. In addition, there is a large cost burden on pain sufferers because the healing process is relatively long (Feldman et al., 2019).

HL Blum's theory or concept suggests that health levels are determined by genetic factors, behavioral factors, environmental factors, and health service factors. These factors are also associated with determinant factors of the disease, including neuropathic pain in diabetes mellitus. Genetically, some genes related to diabetic neuropathy

are ACE (angiotensin-converting enzyme) and MTHFR (methylenetetrahydrofolate reductase) (Rachmantoko et al., 2021).

Influential behavioral factors include diet, physical activity, and mental condition (stress level). Diet affects the incidence of diabetic neuropathy. The results showed that patients with a high carbohydrate diet were at risk of suffering from diabetic neuropathy 4.80 times more than patients with a low carbohydrate diet.8Also, patients with low physical activity patterns are at risk of suffering from diabetic neuropathy 3.57 times than patients with sufficient physical activity patterns (Rahmawati & Hargono, 2018). This is supported by research conducted which concluded that patients with type 2 diabetes mellitus who were given foot exercises experienced a decrease in neuropathy scores and blood sugar levels with ($p = 0.001$) (Yulita et al., 2019).

Environmental factors include work, the majority of respondents with type 2 diabetes mellitus with peripheral neuropathy have jobs as housewives, farmers, and laborers (Wahyuni et al., 2021). This is in line with research by Ramadhan and Hanum, which states that housewives have a greater risk of having type 2 diabetes mellitus. Rahmawati and Hargono also found that the majority of respondents with diabetic neuropathy pain were housewives (Ramadhan & Hanum, 2016).

The main goal of treating neuropathic pain in diabetes mellitus is to eliminate or reduce the feeling of pain. Therefore, the determinant factors of health services also affect diabetic neuropathic pain, one of which is treatment. Studies showed that average blood sugar levels were 267.56 mg/dL for patients on scientific herbal (JS) therapy and 282.95 mg/dL for those on oral antidiabetic (ADO) medication. Post-treatment HbA1c levels were 9.83% for ADO and 10.11% for JS. No significant differences were found between the two therapies in terms of blood sugar and HbA1c levels. (Priadiatna et al., 2021).

Optimal control of blood sugar levels is recommended to approach normoglycemia with HbA1c levels below 7%, although some sources state that blood sugar control has little effect on improving diabetic neuropathy pain. Some pharmacological therapies that can be given include anticonvulsant drugs (pregabalin, gabapentin, carbamazepine, oxcarbazepine, zonizamine, lamotrigine), analgesic drugs (tramadol), antidepressants (amitriptyline, imipramine, duloxetine, nortriptyline), and other topical drugs (capsaicin) (Purwata, 2013).

Currently, one of the therapies used for diabetic neuropathic pain is local anesthetics such as lidocaine. Through specific sodium ion gates on the neuronal membrane, local anesthetic medications impede the delivery of sodium ions, preventing the transmission of nerve impulses (conduction blockade). (Choi et al., 2017). Lidocaine infusion therapy is considered effective for short-term pain treatment, but not very effective for the long term (Zhu et al., 2019). However, in another study, repeated lidocaine infusions over a 4-week period had no significant effect on relieving neuropathic pain, and intravenous lidocaine was associated with many side effects compared to placebo (Purnami et al., 2020).

MATERIAL AND METHODS

This study has received ethical approval from the Faculty of Medicine, Wijaya Kusuma University, Surabaya with approval number 97/SLE/FK/UWKS/2023. This study used an observational analytical design with a cross-sectional approach.The dependent variable was lidocaine therapy in Diabetic Neuropathic Pain (DNP) patients, while independent variables include genetic factors (age, blood type, gender, family history), behavioral factors (stress level, physical activity, education level, smoking, foot care, eating habits), health care factors (treatment compliance, type of medication, patient referral, duration of diabetes), environmental factors (alternative therapy, level of knowledge, socioeconomic status, type of employment), and APGAR and SCREEM scores.

This study involved 244 patients with diabetic neuropathic pain who received lidocaine injections at the Bhayangkara Hospital Pusdik Brimob Watukosek between August 2020 and April 2021. Sampling was carried out using the consecutive sampling method based on medical records during peak visits to the pain clinic. Inclusion criteria were patients who received lidocaine injections and provided written consent. Exclusion criteria included pregnancy or breastfeeding, lidocaine allergy, and refusal to provide consent.

This analysis included the distribution and percentage of variables, with a comparison between patients with reduced pain and those with persistent pain using the Logistic Regression test, followed by contingency coefficient analysis using SPSS version 27 to evaluate the strength of the relationship.

RESULTS

Table 1 shows that the highest proportion of dependent variables is in the DNP category (61.9%) compared to the non-DNP category (38.1%). Among the independent variables, the largest proportion of genetic factors is in individuals over 40 years of age (74.6%), blood type O (57.8%), female gender (79.5%), and those with no family history (71.7%). In behavioral factors, the highest proportion was found in individuals with high stress levels (>20) (52%), low physical activity (<600 MET) (59.4%), education level below junior high school (66.8%), non-smokers (59.4%), good foot care (70.9%), and risky eating habits (77%). For health service factors, the highest proportion was in those who received regular treatment (52%), use of one type of medication (90.2%), patients who were never referred (94.7%), and those who had diabetes mellitus for less than 5 years (56.6%). In environmental factors, the highest proportion was found in those who used alternative therapy (60.7%), had low knowledge levels (63.5%), had socioeconomic status below the regional minimum wage (95.1%), and were

unemployed (62.3%). Regarding quality of life, the highest APGAR score was in the range of 8–10 (53.7%), and the highest SCREEM score was in the range of 5–6 (54.9%).

Genetic Factors

Table 2 shows that, among genetic factors, age category (0.047) and family history (0.004) were statistically significant, while blood type (0.817) and gender (0.721) were not significant.

Behavioral Factors

Table 2 shows that, among the behavioral factors, significant results were found in the categories of physical activity (0.010), education level (0.001), and smoking (<0.001). Meanwhile, insignificant results were found in stress level (0.543), foot care (0.669), and eating habits (0.614).

Health Service Factors

Table 2 also shows that in the health service factor, significant results were found in the category of regularity of treatment (<0.001). However, insignificant results were found in the type of treatment (0.388), patient referral (0.228), and duration of diabetes mellitus (0.771).

Environmental Factors

Finally, Table 2 shows that, in terms of environmental factors, significant results were observed in the alternative therapy category (<0.001), while knowledge level (0.081), socioeconomic status (0.764), and type of employment (0.407) were not statistically significant.

Quality of Life

Table 2 shows significant results for quality of life with SCREEM (0.036) compared to APGAR (0.414) in relation to diabetic neuropathic pain.

DISCUSSION

Genetic Factors

The results of the study showed significant genetic factors in the age category and family history, this is because type 2 diabetes mellitus generally appears at the age of 40 years and over due to decreased body function and increased glucose intolerance. Most elderly people with diabetes experience Diabetic Neuropathic Pain (DNP) which is associated with increased nerve inflammation, oxidative stress, ischemia, and proinflammatory changes, all of which can worsen with age (Hagen & Ousman, 2021). According to previous research findings, patients with type 2 diabetes have a higher risk of developing DNP if they are older, and their age is non-linearly positively correlated with the likelihood of developing DNP (Mao et al., 2019).

This study is consistent with research that found that individuals without a family history of diabetes have a lower risk of developing polyneuropathy compared to those with a first-degree relative with type 2 diabetes. This association was detected through thermography, indicating a strong influence of genetic factors. Family history of diabetes is associated with genetic polymorphisms (eg, angiotensin-converting enzyme) and hundreds of gene expression profiles associated with diabetic neuropathy (Leyva, 2020). A history of diabetes in a first-degree relative was a significant risk factor for neuropathy ($P < 0.001$), with a higher incidence in these patients. This suggests a possible genetic influence, supported by studies highlighting the role of genes such as VEGGF in the development of neuropathy (Rad et al., 2020).

The results of the study on genetic factors that were not significant in blood type and gender, this is because the difference in the development of neuropathy between men and women is influenced by hormonal imbalance. Thyroid disorders (hypo / hyperthyroidism) can trigger neuropathy through metabolic mechanisms and nerve compression. Progesterone plays a role in myelin regeneration. This study shows that women are more susceptible to neuropathy than men, so gender is an important predictor (Rad et al., 2020). The effectiveness of reducing VAS scores was 80% higher in the female group than in the male group. Testosterone levels were higher in men than in women. Through satellite cell activation and stimulation of protein synthesis, testosterone increases muscle mass and strength (Purnami et al., 2020; Wijaya et al., 2021).

Mandal et al.'s study found a greater risk of type 2 diabetes mellitus in those with AB+ blood group (HR 1.26 [95% CI 1.02, 1.57]). The study concluded that people with blood group O had a lower risk of developing type 2 diabetes mellitus. In another study, AB blood group was more common in people with diabetes mellitus compared to the control group. Another study stated that ABO and Rh blood groups in diabetes mellitus, found strong indications of a relationship between diabetes mellitus and blood group, especially in blood groups A, AB, and Rh-positive (Mandal et al., 2018).

Behavioral Factors

The results of behavioral factor research showed significant results in the categories of physical activity, education level and smoking habits. Research by Suhita et al. revealed that the higher the physical activity, the greater the blood sugar needed by the muscles to produce energy. So that the sugar in the blood that is stored will decrease. Lack of physical activity results in a positive energy balance stored in adipose tissue because energy intake exceeds energy expenditure (Suhita et al., 2021).

The level of education has a significant effect on reducing the chances of occurrence. This is related to the level of understanding and knowledge about the risk of diabetes mellitus, the group that did not attend school until graduating from elementary school had a low understanding and knowledge about the risk of diabetes mellitus,

while the group that graduated from high school to college had a high understanding and knowledge about the risk of diabetes mellitus (Kementrian kesehatan RI, 2018).

Smoking can worsen diabetic neuropathy (DN) through oxidative stress, inflammation, and endothelial dysfunction. Several studies have shown that smoking is a major risk factor for DN in people with T2D, especially those who have been diagnosed for more than five years. However, the relationship between smoking and DN is still unclear, so further research is needed to understand its impact, including the impact of smoking cessation (Walicka et al., 2024).

Meanwhile, the non-significant ones were in the categories of stress level, foot care, and eating habits. The study is inconsistent with the results of previous studies which stated that stress levels are related to DNP. The mechanism of stress can worsen neuropathic pain through the mechanism of integrating information related to the influence of stress with nociceptive information in the central nucleus of the amygdala (Dewangga & Andiani, 2023). Stress is a stimulus or situation that causes physical or psychological pressure, requiring adaptation and handling. According to the American Institute of Stress, there is no universal definition because individual responses to stress vary. The National Association of School Psychologists defines stress as a subjective feeling of discomfort that is felt differently by each person (Pratiwi et al., 2016).

Diabetic foot care behaviors (DFCBs) include actions such as foot examination, hygiene, nail care, wound management, and footwear selection. However, lack of patient awareness of diabetic foot complications leads to poor adherence to DFCB. Three studies have shown that poor knowledge leads to poor adherence to these behaviors (Woo & Cui, 2023). This study is not in line with the research of Kurnia et al. which showed a significant influence between foot care on symptoms of peripheral neuropathy in patients with diabetes mellitus. Foot care as an effort to prevent complications due to diabetes mellitus is useful in minimizing the risk of symptoms of peripheral neuropathy such as diabetic foot injuries that lead to amputation if not treated properly (Kurnia et al., 2022).

Diabetes mellitus is often triggered by foods containing carbohydrates. There are two types of carbohydrates, namely simple carbohydrates and complex carbohydrates. A low-carbohydrate, high-fiber diet has been shown to reduce hemoglobin A1c by 1-2% in people with type 2 diabetes. Consuming foods with a low glycemic index helps keep blood sugar levels stable.

Health Service Factors

The results of the study showed that in health services, significant results were found in the category of regularity of treatment. Meanwhile, insignificant results were obtained in the categories of drug type, patient referral, and duration of DM.

This study is in line with Rahmawati et al. who showed that regularity of treatment is associated with diabetic neuropathy. Controlling blood sugar levels, especially through instant blood glucose and HbA1c tests, is important to prevent complications. High HbA1c levels are positively associated with an increased risk of diabetic neuropathy (Rahmawati & Hargono, 2018).

Pharmacological therapies that can be given include anticonvulsant drugs (pregabalin, gabapentin, carbamazepine, oxcarbazepine, zonizamine, lamotrigine), analgesic drugs (tramadol), antidepressant drugs (amitriptyline, imipramine, duloxetine, nortriptyline), and other topical drugs (capsaicin) (Purwata, 2013). The use of pain relievers in the sodium diclofenac or paracetamol group in health care facilities based on cost-effective calculations and existing medical service standards shows that the costs used are only based on the perspective of direct medical cost payers related to drug prices based on the perspective of hospitals and the 2020 e-catalog or BPJS, this causes the treatment of diabetic neuropathy pain to be less than optimal (Sari & Faizah, 2020).

A variety of drugs in the treatment of DNP, either given alone or in combination, have been shown to significantly reduce neuropathic pain compared with placebo in randomized studies, but the reduction is still inadequate in most patients. Various pharmacological treatments have been used to reduce pain in patients with DNP. These include antidepressants, anticonvulsants, analgesics, and topical medications (Hidayati, 2022).

The conditions in our society, treatment for diabetic neuropathy pain therapy, many use traditional therapy, perhaps because of the desire to recover quickly and culture or ancestral experience, although a study also stated that there is no significant relationship between culture and the use of traditional medicine in patients with diabetes mellitus. Complementary, alternative, and traditional medicine is one of the lists of health services that are not covered by BPJS, this also adds to the problems for patients and their families (Piter, 2016).

Environmental Factors

The results of the study showed that environmental factors were significant in the alternative therapy category, while the level of knowledge, socio-economics, and type of work were not significant.

Specific therapies based on pain mechanisms may differ for each person. Pharmacological treatments (pregabalin, gabapentin, opioids, venflaxin, etc.) and non-pharmacological treatments (swimming, acupuncture, physiotherapy) are both included in pain management. In general, therapies for diabetic neuropathy aim to reduce peripheral and central nerve excitability by modulating ion channels and synaptic transmission, and enhancing endogenous inhibitory mechanisms (Putri, 2021).

Knowledge about diabetes helps patients understand the importance of self-care, such as diet, physical activity, and medication management. Studies show that patients with higher levels of knowledge tend to be more skilled at managing blood glucose levels, reducing the risk of long-term complications, and improving adherence to

treatment. In addition, good understanding allows patients to make better decisions in critical situations, such as managing hypoglycemia or when sick (Ferreira et al., 2024).
Employment status can affect the success of diabetes treatment through several mechanisms, such as access to care, stress levels, and self-management. Diabetic patients with stable employment often have better access to health insurance and regular medical care (American Diabetes Association, 2024).

Quality of life

The results of the study on quality of life showed a significant relationship between SCREEM and APGAR in patients with diabetic neuropathic pain. This is in line with Suardana's study which found no significant relationship between family support and quality of life in diabetic patients. However, this is different from Sriyani et al's study which found a significant positive relationship between family function and quality of life in diabetic patients at the Parungponteng Health Center (Sriyani & Mulyana, 2023).
Family support is a key component in building family functioning, as assessed by the APGAR score. Functioning families tend to have a better quality of life, especially in social relationships, while dysfunctional families tend to have a lower quality of life (Oktowaty et al., 2018).
Pathological function can be assessed using SCREEM, which includes social interaction, cultural background (eg, Javanese ethnicity), religious adherence, economic stability, education (adherence to medication and routine check-ups), and medical access (health insurance and access to clinics). The family showed good knowledge of the patient's condition, with the patient complying with medication and routine check-ups (Zulfatul Afifah et al., 2023). Family-Based Diabetes Self-Management Education (DSME) has been shown to improve quality of life by enhancing self-care through nurse-led education for patients and families (Hendrico et al., 2025).

Effectiveness of Lidocaine Therapy in DNP Patients

Administration of painkiller therapy is needed in patients with diabetic neuropathy pain that does not improve with single painkiller therapy. If administration of single painkiller therapy in patients with diabetic neuropathy improves the condition, then combination painkiller therapy is not needed (Tambirang et al., 2019). Lidocaine has been proven to be useful in treating acute pain, but lidocaine as an analgesic is very dose dependent, meaning that the ability of lidocaine to treat pain is very dependent on the dose of lidocaine given (Azza et al., 2020).
Lidocaine and its active metabolites interact by blocking the sodium gate, thus inhibiting sodium entry. Sodium that cannot enter will inhibit the depolarization process in the peripheral nervous system, thereby reducing ectopic impulses from afferent nerve cells and inhibiting the dorsal horn polysynaptic reflex in the spinal cord, which will inhibit the transmission of pain impulses without blocking normal conduction (Azza et al., 2020).
Lidocaine is a local anesthetic drug that when administered intravenously has been shown to provide analgesic, antihyperalgesic, and anti-inflammatory effects (Daykin, 2017). Lidocaine has a specific mechanism that is able to reduce excitation of the peripheral nervous system, thereby reducing the pain transmission process (Sipahutar et al., 2013)
Previous studies have shown that lidocaine injection is safe and effective in controlling neuropathic pain, and subcutaneous lidocaine infusion is also effective in some cancer patients and is well tolerated. Studies using subcutaneous lidocaine infusion have shown effectiveness at levels of 100-160 mg/hour. Lidocaine shows anti-pain effects on body pain and neuropathic pain, by producing stimulation of impaired neurons (Harsa et al., 2025).

CONCLUSION

Genetic factors that showed significant results were age and family history categories. Among behavioral factors, significant results were found in the categories of education level, physical activity, and smoking habits. In terms of health services, significant results were found in the category of regularity of treatment, and for environmental factors, significant results were found in the category of alternative therapy.
The results of logistic regression analysis, the influencing factors are in accordance with the concept of HL. Blum on the effectiveness of the use of lidocaine local anesthetic therapy by 50%. Variables that show trends cannot be used as evidence of a statistically strong relationship but can be further explored with a larger sample or additional analysis methods.

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Authors Contribution

Andiani Andiani and Sulistiawati Sulistiawati have given substantial contributions to the conception, methodology and the design of the manuscript, Lilik Djuari, Hanik Badriyah Hidayati and Kuntaman Kuntaman performing analysis and interpretation of the data. All authors have participated to drafting the manuscript, R. Mohamad Javier revised it critically. All authors read and approved the final version of the manuscript.
All authors contributed equally to the manuscript and read and approved the final version of the manuscript.

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Ethical Approval
This study has received ethical approval from the Faculty of Medicine, Wijaya Kusuma University, Surabaya with approval number 97/SLE/FK/UWKS/2023. The study protocol ensured respect for human dignity, safety, and well-being throughout the research process.

Data Availability Statement
The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supplementary files

Table 1. Respondent Characteristics

Variables		**Category**	**n**	**%**	**Mean±SD**
Dependent	Lidocaine Therapy	Reduced pain	151	61.9	1.38±0.487
		Persistent pain	93	38.1	
Independent					
Genetic Factors	Age	>40 Years	182	74.6	1.22±0.436
		< 40 Years	62	25.4	
	Blood Type	O	141	57.8	1.42±0.495
		A, B, AB	103	42.2	

	Gender	Female	194	79.5	1.20±0.404
		Male	50	20.5	
	Family History	No	175	71.7	1.28±0.451
		Yes	69	28.3	
Behaviors Factors	Stress Level	High Stress (>20)	127	52	1.48±0.501
		Low Stress (<20)	117	48	
	Physical Activity	Less <600 MET	145	59.4	1.41±0.492
		Enough >600 MET	99	40.6	
	Level of education	Did Not Graduate from Junior High School	163	66.8	1.33±0.472
		Minimum Junior High School Graduate	81	33.2	
	Smoke	Yes	99	40.6	1.59±0.492
		No	145	59.4	
	Foot Care	Bad	71	29.1	1.71±0.455
		Good	173	70.9	
	Eating Habits	At risk	188	77	1.23±0.421
		No Risk	56	23	
Health Service Factors	Regularity of Treatment	Irregular	117	48	1.52±0.501
		Regular	127	52	
	Types of Drugs	Combination	24	9.8	1.90±0.298
		Single	220	90.2	
	Patient Referrals	Once	13	5.3	1.95±0.225
		Never	231	94.7	
	Long time suffering from DM	>5 Years	106	43.4	1.57±0.497
		< 5 Years	138	56.6	
Environmental Factors	Alternative Therapy	Do	148	60.7	1.39±0.490
		Do not do	96	39.3	
	Level of Knowledge	At risk (Score 0-50)	155	63.5	1.36±0.482
		No Risk (Score 51-100)	89	36.5	
	Socio-Economic	Below UMK	232	95.1	1.05±0.217
		Above UMK	12	4.9	
	Type of work	Doesn't work	152	62.3	1.38±0.486
		Work	92	37.7	
Quality of life	APGAR	0-7	113	46.3	1.54±0.500
		8-10	131	53.7	
	SCREEM	1-4	110	45.1	1.55±0.499
		5-6	134	54.9	

Table 2. p-value and Exp(B) of each variable on the effectiveness of lidocaine therapy for DNP patients.

Variable	**Category**	**p-value**	**Exp(B)**
Genetic Factors	Age	0.047*	1.847
	Blood type	0.817	0.937
	Gender	0.721	1.129
	Family history	0.004*	0.394
Behavioral Factors	Stress level	0.543	0.828
	Physical activity	0.010*	2.186
	Level of education	0.001*	2.697
	Smoke	< 0.001*	4.783
	Foot care	0.669	1.153
	Eating habits	0.614	0.836
Health Service Factors	Regularity of treatment	< 0.001*	2.909
	Types of drugs	0.388	1.608
	Patient referrals	0.228	2.804
	Long time suffering from DM	0.771	0.920
Environmental Factors	Alternative therapy	< 0.001*	3.130

	Level of Knowledge	0.081	1.659
	Socio-Economic	0.764	0.824
	Type of work	0.407	1.271
Quality of Life	APGAR	0.414	1.244
	SCREEM	0.036*	1.761

Note: *Significant (p < 0,05)