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Evaluation of Relationship Between Body Mass Index and Experimental Pain Responses in a Young Population In Northern Nigeria

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ABSTRACT

Pain perception has been shown to differ between patients with different gender, race and culture. In addition, it has been suggested that obesity influences pain perception, and can be a risk factor for increase pain perception later in life. The aim of this study was to investigate the relationship between obesity and pain perception among a young population in Zaria, Northern Nigeria. One hundred and thirty-two (132) apparently healthy subjects between the ages of 12 to 20 years were assessed for pain using the cold pressor test and ischemic pain models. Subjects also filled a self-reported questionnaire on physical activity. Data were presented as mean ± SD. Differences and statistical significance between the means was determined by t-test for sex differences, while effect of BMI on pain responses was analyzed using ANOVA. Values of $p \leq 0.05$ were considered significant. Result of this study showed that obese subjects had a significantly lower cold pressor pain threshold than non-obese subjects, but no statistically significant difference was observed on cold pressor pain tolerance. Ischemic pain response on the other hand, showed no statistically significant variation between all the groups tested. The study indicates that there is a relationship between obesity and pain perception among a young Nigerian population in Zaria, Nigeria.

Key words: *Pain perception, Body mass index, Cold pressor test, Ischemic pain, Exercise, Obesity*

INTRODUCTION

Pain serves a protective role that alerts an individual to injury from the environment or from within. A multi-dimensional sensory experience that is intrinsically unpleasant and associated with hurting and soreness. Pain can be adaptive or maladaptive. Adaptive pain contributes to survival by protecting the individual from injury or promoting healing when injury has occurred (symptomatic pain), maladaptive pain on the other hand, is an expression of the pathologic operation of the nervous system (pain as a disease) (Woolf 2004). According to the International Association for the Study of Pain (IASP) task force on taxonomy, pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (Kumar and Elavarasi 2016).

The experience of pain is characterised by robust individual differences. Inter-individual variability in the experience of pain is modified by interactions among numerous biopsycho-social factors, including genetic

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influences. There is a high degree of individual variation in pain, very likely due to complex environmental and multiple genetic factors (James 2013). A number of genes play critical role in determining pain sensitivity, pain reporting and susceptibility to developing chronic pain.

It has been reported that two-thirds of the patients that report low back pain has an elevated body mass index (BMI), and is associated with other musculoskeletal pain syndromes due to the presence of a chronic systemic inflammatory state (Seaman 2013). Overweight has been shown to negatively affect the musculoskeletal system disorders (Hozumi et al. 2015), and there is a direct relationship between level of obesity and the likelihood of developing low back pain (Atchison and Vincent 2012). BMI was not found to be related to changes in pain and disability in patients with chronic low back pain after 8 weeks of exercise (Brooks et al. 2013), but BMI at the age of 20 years predicted radiating low back pain later in life (Frilander et al. 2017). Cross sectional studies of persons with radiographic knee osteoarthritis demonstrated a strong link between increased BMI and knee pain, indicating overweight and obesity as a potential cause of knee pain (Rogers and Wilder 2008; Hawamdeh and Ajlouni 2013).

Table 1: Socio-Demographic Characteristics of Subjects

Characteristic	Frequency	Percentage (%)
Sex		
Male	60	45
Female	72	55
Age		
13 – 14 year	45	34
BMI		
Underweight	9	6.8
Normal	83	62.9
Overweight	31	23.5
Obese	9	6.8
Total	132	100
Daily exercise		
No	30	23
Mild	34	26
Moderate	63	49
Severe	3	2
Total	130	100

A study in a Korean community residents showed that increased fat mass and fat/muscle mass ratio were significantly associated with musculoskeletal pain among women. Widespread pain was significantly associated with a high fat/muscle mass ratio. Thus, understanding the relationship between fat mass and pain may provide insights into preventative measures and therapeutic strategies for musculoskeletal pain (Yoo et al. 2014).

Although as clinical syndromes, pain and obesity are significantly associated with each other, research evaluating the relationship between obesity and pain sensitivity has yielded conflicting results. This suggests that the relationship between obesity and pain is not a direct one but mediated by various factors. Such factors include biomechanical/structural changes associated with obesity, inflammatory mediators, mood disturbance, poor sleep and lifestyle issues (Okifuji and Hare 2015).

Studies of experimental pain in humans are free from the confound of disease progression, but can be highly relevant to clinical pain states. Experimental pain studies provide unique insight into the dimensions of pain and into individual differences in pain responsiveness by controlling different aspects of pain-eliciting stimuli and pain measures (Lacourt et al. 2012). As such, research into differences in pain perception among non-pain sufferers is important. This study evaluates differences in pain perception in response to experimental pain among a young Nigerian population in Zaria, Nigeria.

MATERIALS AND METHODS

Normal healthy volunteers were the subjects for this study. Evaluation was carried out using observational cross-sectional study. The subjects, which were drawn from a young adult population (age 13 to 20 years) were divided into younger group (less than 15 years) and older group (15 years and above). Informed consent was obtained from all the subjects, as well as ethical approval from the Ahmadu Bello University Teaching Hospital Health Research Ethics Committee (ABUTH/HREC/TRG/36) prior to the study. Subjects were excluded if they had prior or present alcohol abuse issues, use daily analgesics, a disorder that would interfere with pain perception and pain report, or any symptoms or signs of any neurological or inflammatory disease that could interfere with pain perception. Responses of each individual subject to pain stimuli were observed and recorded.

Experimental Procedure

The subjects completed questionnaires stating their age, sex, education level, health condition and drugs used (if any), as well as exercise performance and frequency, followed by a brief interview. Pressure pain was conducted first, followed by a 10 minute rest period before conduction of cold-pressor and ischaemic pain procedures in separate sessions, to avoid carry-over effect. Subjects were randomly assigned to one of three possible testing orders. BMI (kg/m^2) was calculated as the ratio of the subject's weight (kg) divided by the square of subject's height (m^2) (Gotfryd et al. 2015).

Cold Pressor Pain

Cold pressor pain is considered to be a method that mimics the effects of chronic conditions effectively because of its unpleasantness, and it has excellent reliability and validity. Each subject immersed their left hand up to the wrist in a container with ice-cold water at 0°C to 2°C. The temperature was maintained by adding ice cubes and monitored by means of a mercury thermometer (de Nazare et al. 2014). The subjects kept the hand in the water for as long as possible, until the pain became intolerable, at which point, they removed their hands. Cold-pressor pain threshold (in seconds) was determined to be the time when the subject say "pain" and tolerance (also in seconds) was recorded when the hand was withdrawn from the water (Rahim-Williams et al. 2007).

Table 2: Sex and Age Differences in BMI for Studied population

	BMI
Sex	
MALE	22.21±0.41*
FEMALE	23.99±0.53#
Age	
<15	22.20±0.54
15 to 20	23.18±0.46

Mean ±SD: # & * mean difference is statistically significant

Ischemic Pain Procedure

Ischemic pain was induced using a modified sub-maximal effort tourniquet procedure (Moore et al. 1979). The left arm was exsanguinated by elevating it above heart level for 30 sec. The arm was then occluded using segmental blood pressure cuff inflated to 200 mmHg. Subjects were asked to perform 20 hand grip exercises of 2 seconds duration at 4 seconds intervals. They were asked to say 'pain' when they first feel pain (threshold) and to continue until the pain becomes intolerable (tolerance). The time (in seconds) for pain threshold and pain tolerance were recorded.

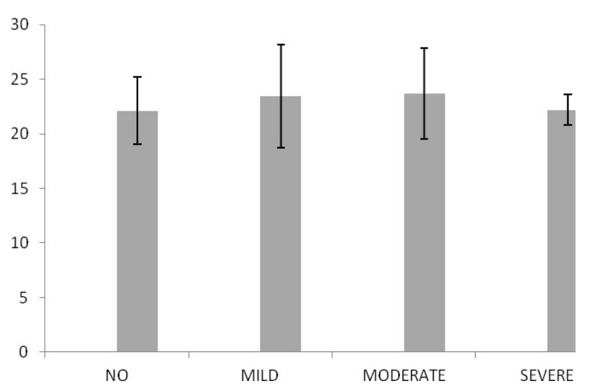

Figure 1: Effect of daily exercise on BMI among the studied population. Not statistically significant between the groups

Data obtained were presented as mean ± standard deviation (SD). Group differences were examined using independent sample t-test and ANOVA. Spearman correlation test was used for correlational analysis. Analysis was carried out using Statistical Product and Service Solution (SPSS, version 23 software, SPSS Inc, Chicago). Values of $P \leq 0.05$ were considered significant.

RESULTS

One hundred and thirty two apparently healthy subjects participated in the study. The mean BMI was 23.29 kg/m^2 (SD: 4.06), with females having higher BMI (23.99 ± 4.5) than males (22.21 ± 3.2). The younger subjects (<15 years) had a higher BMI (23.20 ± 3.6) than the older subjects (15 – 20 years, 23.18 ± 4.3). The socio-demographic characteristic showed that 45% of the participants were males and 55% females (Table 1). Forty-nine percent of the subjects reported that they perform moderate exercise daily, while only 2% reported they performed severe exercise daily (they play football every day). The remaining reported not performing exercise daily. Result of the study shows that BMI is significantly higher in females than in males (Table 1), though age differences in mean BMI do not show significant variation among the age groups. The effect of daily exercise and exercise severity does not significantly influence BMI levels among the studied population (Figure 1), though the no exercise group had the least BMI (22.12 ± 3.1), and moderate exercise group have the highest BMI (23.67 ± 4.2), (P = 0.357). Threshold for cold pressor pain shows BMI dependent variation, with underweight subjects having highest threshold (less pain) and obese subjects having lowest threshold (higher pain) (Figure 2), but cold pressor pain tolerance do not show statistically significant variation, though underweight subjects had the lowest tolerance among the test groups (Figure 2).

Using the sub-maximal effort tourniquet model of ischemic pain, the result showed no statistically significant difference in both pain threshold and tolerance (Figure 3), though underweight subjects had lowest threshold, while overweight subjects had highest tolerance.

Thresholds for both cold pressor pain and ischemic pain showed a weak negative correlation with BMI (Figures 4A and B). Daily exercise activity and/or severity do not significantly affect pain perception in the experimental models used among the study population (Figure 5).

DISCUSSION

The response of healthy individuals to experimentally induced pain was used to investigate relationships between pain sensitivity and dispositional characteristics. Pain sensitivity is the level at which an individual reacts to a noxious stimulus and is measured using controlled experimental stimuli (Astita et al. 2015). Clinical research into the use of systemic opiates for the treatment of postoperative acute pain suggests higher pain scores and greater narcotic requirements in patients with a higher BMI (Grodofsky and Sinha 2014). A study by Moreira-Silva et al. (2013) showed that overweight/obese patients reported higher pain intensity only in shoulders and wrist/hand compared with their lean counterparts. High BMI is reported to significantly increase the likelihood of developing and sustaining foot joint pain (Gay et al. 2014)

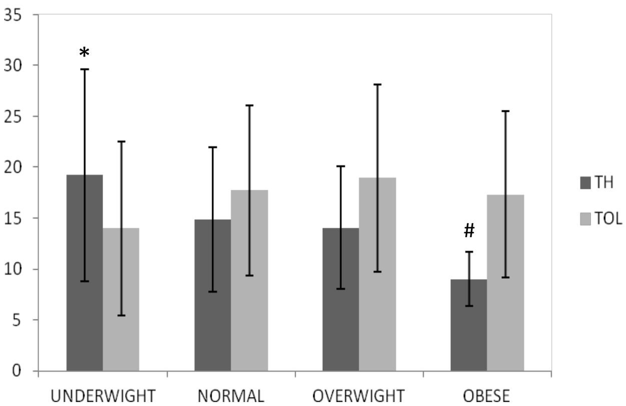

Figure 2: Effect of BMI on cold pressor pain responses. * & # Mean difference is statistically significant (*P*<0.05). TH: threshold. TOL: tolerance

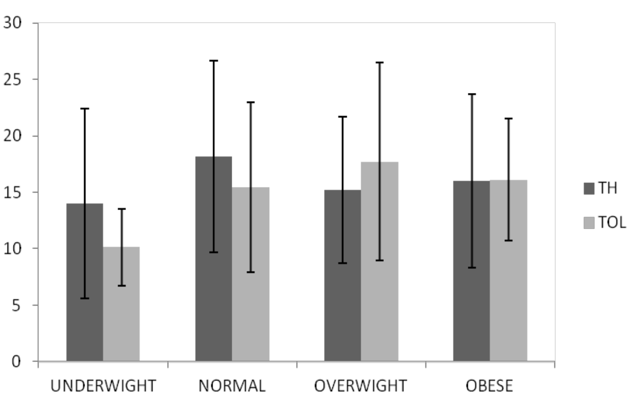

Figure 3: Effect of BMI on ischemic pain responses. Not statistically significant between the groups

The result of this study showed that daily exercise and exercise severity do not significantly affect BMI in the studied population. Weight gain is associated with multiple interrelated factors that promote positive caloric balance coupled with sedentary living. Inadequate sleep and stress also promote obesity by increasing palatable food consumption, due to increased release of ghrelin and other hormones. Less sleep duration can undermine dietary efforts to reduce obesity. Inadequate sleep, stress and sedentary life style promote systemic inflammation, which can be modulated with exercise. Lack of exercise leads to an increase in BMI (Seaman 2013). Unfortunately, this study did not include sleep pattern and/or duration of the studied subjects, which may explain the insignificant effect of exercise on BMI in the studied population. Report showed a consistently lower risk of chronic pain in the low back and neck/shoulders associated with a relatively small amount of physical exercise per week. Independently of physical exercise, persons classified as overweight and obese had a higher risk of chronic pain in the low back and neck/shoulders than persons classified as normal weight. Physical exercise could compensate, to some extent, for the adverse effect of excess body mass on risk of chronic pain in both the low back and neck/shoulders (Nilsen et al. 2011).

Using the cold pressor pain procedure, this study showed a statistically significant weight dependent variation in pain threshold, with underweight subjects having highest threshold (19.22 ± 10.4, less pain) and obese subjects having lowest threshold (9.00 ± 2.6, higher pain) (P = 0.02). Immersion of a region in cold water for a long time lead to deep sense of pain and discomfort (de Nazare et al. 2014). Adiposity affects the metabolic activity of adipose tissue. In low adiposity, adipocytes releases analgesic and anti-inflammatory mediators (adiponectin and interleukin-10). Adiponectin supports insulin sensitivity and mitochondrial biogenesis in skeletal muscle, while interleukin-10 has analgesic and anti-inflammatory immune modulating properties. Increase in adiposity (obesity), on the other hand, is associated with a metabolic shift, such that a systemic chronic inflammatory state develops in certain patients. There is increase in circulating inflammatory mediators, such as C-reactive protein, Tumor Necrosis Factor (TNF) and interleukin-6 (IL-6) in obese individuals than in non-obese controls (Seaman 2013). Macrophages in lean adipose tissue exist in the "M2" or non-activated state. However, with increased adiposity, mast cells, lymphocytes, and macrophages can actively enter adipose tissue, which leads to the transformation of macrophages from M2 to the "M1" or activated state, thus promoting chronic systemic inflammation. Susceptibility to pain in obese individuals may be affected by increases in the concentrations of pro-inflammatory cytokines in the blood (Astita et al. 2015). Overweight and/or obesity were reported to be associated with significantly higher odds for back pain among those aged 50 and above in Finland, Poland, Spain, Russia, and South Africa (Koyanagi et al. 2015). Obese individuals frequently tend to demonstrate limited activities of daily living, which is associated with greater pain sensitivity. Emmanuel et al. (2015) reported a significant association between low back pain and age, experience, place of work, and BMI.

In a study by Kivrak et al. (2016), it was found that depression, BMI, and somatosensory amplification were not the predictors of pain perception. Obesity has been associated with increased secretion of pro-inflammatory cytokines and a decreased secretion of anti-inflammatory cytokines from adipose tissues, and these can lead to systemic inflammation. Inflammation can lead to peripheral and central sensitization in the pain transmission system and result in hyperalgesia and allodynia (Hozumi et al. 2015). Increased adiposity leads to physiologic changes that alter pharmacokinetics such as an increase in cardiac output, a disproportionate increase in adipose tissue and other alterations that affect drug metabolism (Grodofsky and Sinha 2014). Increased IL-1β in the serum significantly predicted enhanced sensitivity to heat pain, while both IL-1β and TNF-α were positively associated with an augmented potency of remifentanil analgesia for heat and cold-induced pain (Doufas et al. 2013).

Using the sub-maximal effort tourniquet model of ischemic pain, the result showed no statistically significant difference in both pain threshold and tolerance, though underweight subjects had lowest threshold while overweight subjects had highest tolerance. Grodofsky and Sinha (2014) reported that while age is associated with slightly lower pain scores, there was no evidence that obese patients have clinically different pain responses. In a study by Tashani et al. (2017), it was reported that obese individuals were more sensitive than non-obese individuals to pressure pain but not thermal pain, and that body sites may vary in their response to different types and intensities of stimuli according to underlying levels of subcutaneous fat. Pain threshold has also been reported to be higher in subjects with BMI >25, showing decreased pain sensitivity in obese people (Petkova et al. 2014)

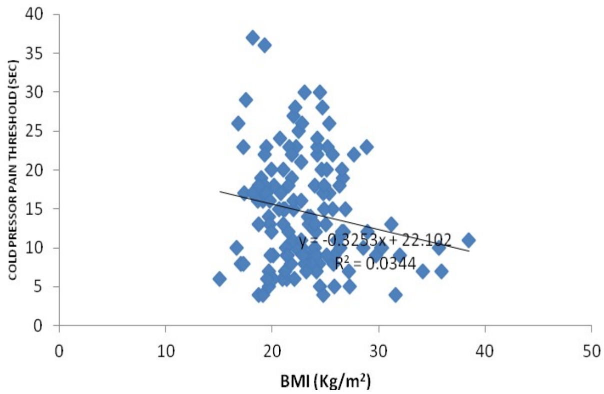

Figure 4A: Negative correlation between BMI and pain perception using cold pressor pain model

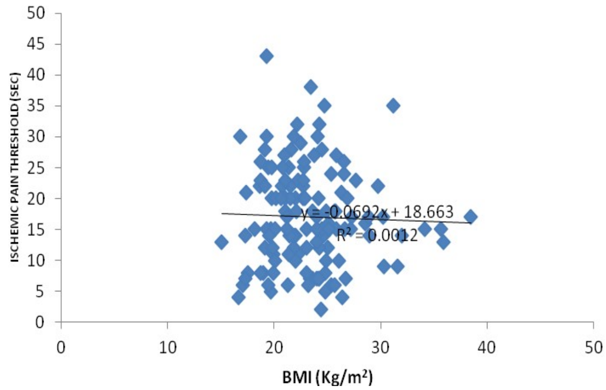

Figure 4B: Negative correlation between BMI and pain perception using ischemic pain model

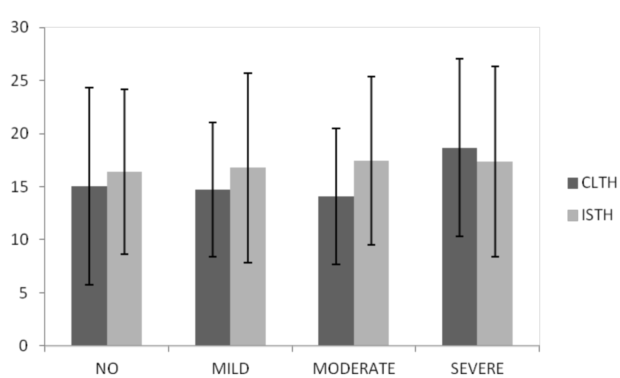

Figure 5: Effect of daily exercise on pain perception. CLTH: Cold pressor pain threshold. ISCH: Ischemic pain Not statistically significant between the groups threshold

Obesity is the sixth most important risk factor contributing to the overall burden of diseases throughout the world. Various population studies suggest that at least two-third cases of hypertension are due to obesity. Health risks associated with obesity include type 2 diabetes mellitus, gall bladder diseases, dyslipidemia, metabolic syndrome, breathlessness, hypertension, coronary artery disease, sleep apnea, stroke, and congestive heart failure. Obesity was linked with glomerulopathy and weight loss by morbidly obese individuals was found to be associated with significant reduction of urinary protein excretion (Saxena et al. 2015). Evidence suggest that changes occurring in the milieu of afferent sensory neurons during inflammation, may augment the potency of μ-agonists either by up-regulation of μ-opioid receptors or by increasing their affinity (Doufas et al. 2013).

Our result could not explain specific physiological mechanisms by which obesity affect experimental pain perception among the studied population, but indicate high BMI as an aggravating factor in pain perception. Further research is required to ascertain how change in BMI affects perception of experimentally induced pain stimulus.

CONCLUSION

The analysis of the effect of BMI on experimental pain perception revealed that high BMI is related to decreased pain threshold among young population in Zaria, Nigeria. Obese subjects in this study were found to have a significantly lower cold pressor pain threshold than underweight subjects, but no difference on cold pressor pain tolerance. Ischemic pain threshold and tolerance showed no statistically significant variation by BMI.

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Conflict of Interest
None declared.

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