

GLOBAL JOURNAL

OF MEDICAL RESEARCH: K

Interdisciplinary

A Review and Emphasis

Impacts of Asthma-Obesity

Highlights

Vigorous Physical Activities

Generalized Linear Mixed Mode

Discovering Thoughts, Inventing Future

VOLUME 15

ISSUE 1

VERSION 1.0



GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY



GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY

VOLUME 15 ISSUE 1 (VER. 1.0)

OPEN ASSOCIATION OF RESEARCH SOCIETY

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GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY

Volume 15 Issue 1 Version 1.0 Year 2015

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Impacts of Asthma-Obesity Association's on Children's Moderate and Vigorous Physical Activities

By Abdulraouf Y. Lamoshi & Lesley E. Cottrell

West Virginia University/ Tripoli Medical Center, United States

Abstract- Background: This study was developed to explore the relationship between asthma and obesity and the impact of that association on children's physical activities. Potential age and gender differences in the association between asthma, obesity, and activity were also examined.

Methods: Children were recruited from outpatient physician clinics to participate in a cross-sectional study. Child body mass index percentile and asthma severity were clinically assessed. Children's physical activity was assessed through parent report and assigned appropriate metabolic equivalent task (MET) scores.

Results: 75 children participated in the study. Regardless of their asthmatic and weight statuses, boys and girls significantly differed based on their average MET scores ($p = .007$), respectively. Younger, mildly asthmatic children had significantly higher MET scores than older, mildly asthmatics ($p < .05$); younger, severe asthmatics had moderately higher average MET scores than older, severe asthmatics ($p < .05$).

Conclusion: Young asthmatic children and boys overall are more physically active than the older, asthmatic children and girls overall, respectively.

Keywords: *asthma-obesity association, moderate and vigorous physical activities, children.*

GJMR-K Classification: *NLMC Code: WD 300*



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Impacts of Asthma-Obesity Association's on Children's Moderate and Vigorous Physical Activities

Abdulraouf Y. Lamoshi ^α & Lesley E. Cottrell ^σ

Abstract - Background: This study was developed to explore the relationship between asthma and obesity and the impact of that association on children's physical activities. Potential age and gender differences in the association between asthma, obesity, and activity were also examined.

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Conclusion: Young asthmatic children and boys overall are more physically active than the older, asthmatic children and girls overall, respectively. Established age and gender differences in physical activity may be found more readily among specific samples of children, particularly those with asthma.

Keywords: asthma-obesity association, moderate and vigorous physical activities, children.

1. INTRODUCTION

Many studies show that asthma and obesity are important public health problems because of their high prevalence among children; these medical problems affect the quality of life of the patients and consume significant amounts of money to provide the necessary medical care [22]. Researchers have postulated and established a positive association between obesity and asthma; however, a definitive causal relationship and an understanding of which condition comes first remain unobvious [4,16]. Moreover, patients who are obese and have asthma symptoms do not respond in the same manner to asthma medications as non obese patients [7].

The main asthma-obesity potential mechanism is the significant pressure from the overall weight gain. Overweight children carry extra pounds making it harder for some to be physically active, particularly asthmatic children [24]. Tidal volume and functional residual capacity also decrease due to mechanical impact of the fat tissue [4]. This, in turn, affects the lung function especially when the body demands for oxygen increase [4]. Obesity also leads to loss of the tightening of gastroesophageal sphincter which causes gastroesophageal reflux, in turn leading to aspiration of the stomach contents [14]. As a result the lung airways get constricted which makes the respiratory process a hard task [4]. The other potential mechanism is that increase in body weight causes the immune system to secrete some inflammatory substances which could result in over reaction of the airways that in turn leads to constriction of those air passages and difficulty in breathing [3]. Other targeted mechanisms for the association between asthma and obesity are related to immunological changes, dietary modifications, genetic factors, and activated sex hormones [4,14].

Early teen-age girls' asthma symptoms and obesity risk measured by body mass index (BMI) are significantly associated [6]. A similar conclusion has been drawn by another study which stated that girls who develop early menarche are at a higher risk of developing asthma and obesity [8]. Only obese or overweight girls between 6 and 11 years are seven times at a higher risk of developing asthma [19]. Asthma prevalence was higher among girls who are younger than 11 years and developed early puberty [4]. There is some controversy about which gender is at a higher risk in some studies' conclusions. However, they are more inclined toward the girls' side, and the difference in these studies could be due to the children's ages at which the association was reported [4,21,22]. The prevalence of obesity and overweight among children was 6.87% in boys and 9.5% in girls [12]. The most acceptable hypothesis for the higher prevalence of asthma among females is that adipose tissue's aromatase converts androgens into estrogens, which in turn change lung development and airway tone responsiveness at the age of puberty [4].

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Asthma-obesity association has negative impact on children's physical activity where children with asthma have higher mean BMI (20.78 vs. 18.82) and higher rates of obesity (21.4% vs. 6.6%); children with asthma reported fewer physical activities than the nonasthma group (median 4 per day vs. 6 per day) [9]. Also, they found that asthma is the strongest predictor of lower activity scores, and the asthma group has higher levels of emotional problems and, within this group, more active children have better mental status [9]. Parents in the asthma group identified the child's health as an obstacle to exercise (60.7% vs. 11%) and the same is true of children (66.1% vs. 11.5%) [9]. Asthma was identified as a barrier to exercise by parents and children [25]. Strategies to promote exercise within pediatric asthma care are needed to protect both mental and physical health [5]. Furthermore, physical activity is influenced negatively by asthma and obesity, and it can become worse because of their additive effect [20]. However, there are some other studies which show no association between asthma and physical activity [20] or asthmatic children do more physical activities than non asthmatic children [17,18].

Types of physical activity, and their MET scores, are subjected to change when children are divided into two groups, 6 -9 years and 10- 14 years. The first group is more inclined to participate in anaerobic activities, and the older children tend to participate in more organized activities [23]. Children between ages of 6 to 11 year spent more time doing moderate to vigorous physical activities than older children who are between ages of 12 to 15 years, and girls spent less time doing moderate to vigorous physical activities than boys of the same age [1]. Guerra et al.'s study finding could be one potential indicator of decreasing physical activities between these groups where it showed that BMI increases progressively with age after the age of 6 years until the age of 11 years [10].

In general, the concomitant increase in prevalence of both disorders in children has led to interest in the relationship between these two epidemics [22]. The debate about the nature of the asthma-obesity relationship is ongoing and some possible explanations should be considered to comprehend the reality of that association [14]. However, working to decrease the BMI would improve the status of asthma patients in terms of frequencies of the attacks, need to treatment, and side effects of those medications [6]. Based on what stated above, meticulous exploration of asthma-obesity association effect on children physical activities could be the first step to manage this issue. We don't know how the combination of being asthmatic and obese might influence physical activity? What are the gaps based on the current research for these three variables and why should we look at them now?

The research aspect of this study aimed to provide several benefits to the research community and

society as a whole. The main goal was to will identify ways in which childhood obesity and/or asthma, age, and gender impacts a child's physical.

II. METHODS

An observational cross-sectional study of 145 children (7-12 years) was conducted to examine the impact of asthma obesity association on children's physical activities. This study was a secondary analysis of a larger cross sectional clinical study that examined children's the psychological, physiological, and cognitive impact of obesity and asthma. The ultimate goal of this work is to decrease asthma and obesity prevalence and maintain or increase physical activity among all children, regardless of asthma or obesity condition. The short-term goal of this study was to examine obesity-asthma association impact on children physical activities. Based on the existing literature, we hypothesis that:

1. asthma and obesity are associated together;
2. the amount of physical activities will be less among asthmatic children;
3. the amount of physical activity will be less among children who are obese; and
4. asthma and obesity have will have an additive effect on children's physical activity

This study was designed to explore the impact of asthma-obesity association on children's physical activities. This topic has not been examined in this sense closely and thoroughly before.

Measures: In this study, we focused on certain items in some questionnaires such as how often the children do exercise per week, from parents' perspective, and severity of asthma based on number asthmatic attacks during the daytimes and at nighttimes per week and month. From pulmonary function test's items, forced expiratory volume of the first second (FEV1) was used to categorize the severity of asthma from laboratory view. Reviewing the history form and case report form show the BMI% and whether the children have been diagnosed as asthmatic before or not.

Study variables were gathered by survey and clinical assessment during a scheduled clinic visit. The following measures were incorporated into the present study:

Childhood Obesity: Children's height (inches) and weight (pounds) measured using the SECA Road Rod stadiometer (78"/200 cm) and the SECA 840 Personal Digital Scale. Children asked to remove their shoes and jackets prior to assessing their height and weight. Body mass index for each child calculated using the recommended equation by the Centers for Disease Control. All weight percentile categories (e.g., normal, overweight, obese) were based on the age and gender, specific growth charts recommended by the Centers for

Disease Control and Prevention (CDC) [11]. We used BMI% to classify the participants into: < 5th percentile under weight, 5-85th percentile normal weight, 85-95th percentile are overweight, and > 95th percentile are obese.

Childhood Asthma : The standard lung function test was carried out according to the recommended standards. The main value which was used in this study is the forced expiratory volume in one second (FEV1). FEV1 < 60 is severe asthma, 60-80 moderate asthma, and > 80 mild asthma and normal.

Asthma Severity : Asthma Assessment Form was used to assess the severity of asthma symptoms in terms of number of attacks per week during the day time and night time. Mild: 1-6 days /week and 3-4 nights/month, moderate: daily during days and 5-9 nights/ month, and severe: continuous during daytime and 10 nights/ month.

Children physical activities were collected from parents who were asked to recall what their children's activities were over the past week. MET is "the ratio of the metabolic rate of the average person while seated and resting, to the metabolic rate of a particular person while performing some task" [2]. MET stands for Metabolic Equivalents of Task. One MET is "equivalent to a metabolic rate consuming: 3.5 milliliters of oxygen or 1 kilocalorie, per kilogram of body weight per minute" [2]. For that purpose we used the CDC and American College of Sports Medicine (ACSM) guidelines for the definition of the activities, 3-6 METs are moderate and greater than 6 METs are vigorous (Martin, Morrow, Jackson, and Dunn, 2000), Table 2. MET scores for children's physical activities is measured based on this form. Physical activities score is calculated by multiplying the times of each activity by hours of each activity by the assigned MET value for that activity. The sum of the scores gave the overall value for each activity over the last week before filling the form [15].

Children's age was collected as a continuous variable and later grouped into two categories younger (7-10 years) and older (11-13 years).

Statistical Analysis: SPSS for Windows Version 20.0 was used for data analysis. Descriptive statistics were summarized as mean (with SD) and frequency (%). Chi-square test and Student's t test were used to compare

differences between groups. MANOVA analysis was conducted with total MET's scores as the dependent variable and group (asthma vs. nonasthma) and BMI% (healthy weight vs. overweight and obese) as independent variables. An interaction between asthmatic status and BMI% of the children was created and placed in the model as an independent variable. Basic model-fitting techniques for regression analysis, including goodness-of-fit assessment and regression diagnostics (e.g., residual analysis, detection of influential cases, and check for multicollinearity) were applied. Because physical activity data were not distributed normally, two outliers were removed before t tests and regression analyses were carried out. For all tests, p-values of 0.05 were considered statistically significant. Approval was obtained from the Institutional Review Board.

III. RESULTS

Sample: A total of 145 children were recruited into the study; 75 children completed the physical activity data. Fifty-eight percent (43) of the sample was males, and the majority of the sample was Caucasian (85.5%). Seventy-nine (54.5%) children were of healthy weights; 66 (45.5%) were either obese or overweight. Seventy-seven (53.1%) were non-asthmatics and 68 (46.9%) were asthmatics (28 mild, 33 moderate, and 7 severe).

Obesity and Asthma Prevalence: Out of the 75 children who completed the physical activity form 41 (54.7%) were non-asthmatic, 15 (20%) were mild asthmatics, 14 (18.7%) were moderate asthmatics, and 5 (6.7%) were severe asthmatics. In terms of body composition, 43 (58 %) were under- or healthy weight and 31 (42%) were overweight or obese. Based on gender, more girls (48.39%) were asthmatic than boys (44.19%); on the other hand, boys (44.19%) were more likely to be overweight or obese than girls (31.71%). When grouped by their asthma and body composition status, 29 (38.7%) were non-asthmatic and non-obese/overweight, 18 (24%) were non-asthmatic and obese/overweight, 15 (20%) were asthmatic and non-obese/overweight, and 13 (17.3%) were asthmatic and obese/overweight, Table 1. The mean MET score of all children was 49.82 (SE = 4.62).

Table 1 : Participants' Demographic

Characteristic	Participants' # (%)
Gender	
Boys	43 (58%)
Girls	31 (42%)
Age	9.59 year
Group 1 (7-10 years)	44 (59.5%)
Group 2 (11-13 years)	30 (40.5%)
Race	
White	65 (87.8 %)

Black	3 (4.1%)
Hispanic	2 (2.7%)
Asian	2 (2.7%)
Family history of Asthma	
Yes	29 (38.6%)
No	42 (56%)
Missing	4 (5.4%)
Asthma	
Yes	34 (45.3%)
No	41 (54.7%)
Height	49.34 (9.07)
Weight	89.78 (39.86)
BMI %	60.51(31.74)

Obesity and Asthmatics and Physical Activity: Regardless of their asthmatic and weight statuses, boys and girls significantly differed based on their average MET scores (63.32 vs. 43.77) respectively ($F = 7.87$, $P = .007$) (Figure 1). Concerning the age, there was no significant difference in MET scores where the younger group had insignificantly higher MET scores (60.97 vs. 43.09) ($F = 1.05$, $P = .311$). Asthmatic participants, regardless of the severity, did not differ in terms of their MET scores from non-asthmatics: non-asthmatics'

mean MET score was 37.27 (SE = 6.47), mild asthmatics' mean MET score was 61.03 (SE = 11.03), moderate asthmatics' mean MET score was 64.26 (SE = 11.25), and severe asthmatics' mean MET score was 63.81 (SE = 18.59) ($P = .284$). Overweight and obese children, regardless of their asthma status, had slightly higher mean MET scores than the healthy weight children ($X = 56.93$ and $X = 51.70$ respectively) but this was not a significant difference ($p = .331$).

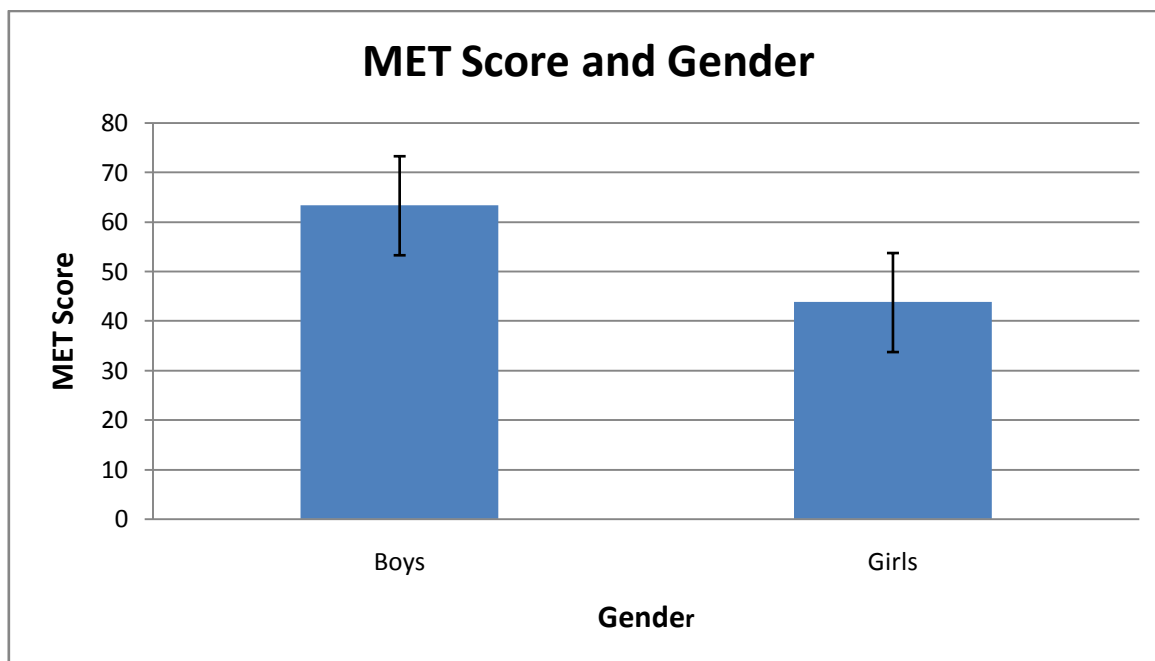


Figure 1 : Metabolic Equivalent Task Score of the Participants According to Gender

Analysis of the Composite Group: An interaction effect between participant age and asthma diagnosis was found with regard to average MET scores ($F = 3.08$, $P = .036$). Specifically, younger mildly asthmatic children had significantly higher MET scores than older mildly asthmatics (81.25 vs. 20.60, $p < .05$). Younger severe asthmatics also had moderately higher average MET scores than older severe asthmatics (65.71 vs. 60.00, $p < .05$), Figure 2.

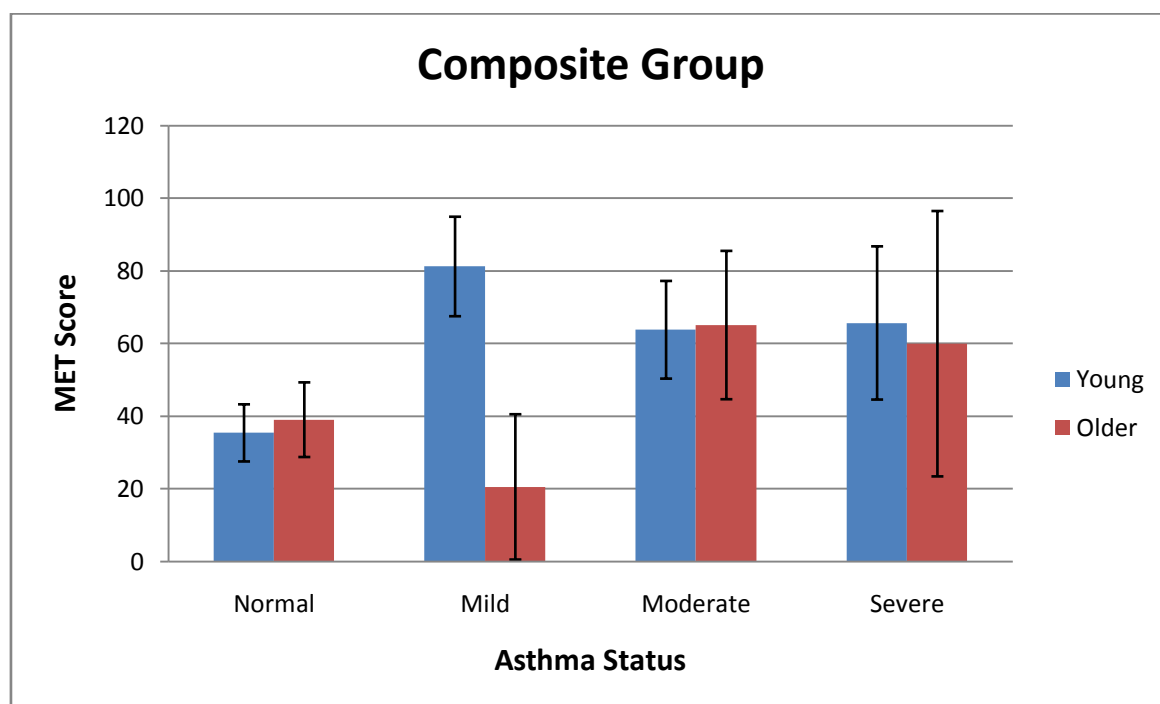


Figure 2 : Metabolic Equivalent Task Score of the Participants According to the Age and Asthma Statuses

IV. DISCUSSION

The main findings of this study were that mild and severe asthmatic young children and boys, in general, were significantly involved in moderate to

vigorous physical activity than mild and severe asthmatic older children and girls, respectively. BMI alone had no significant influence on children's moderate to vigorous physical activities.

Table 2 : The Survey was used to Assess Children Moderate and Vigorous Physical Activities

Activities' List	MET
1. Ride bike, Skate (roller, inline, ice, skateboard)	4
2. T-ball/Baseball/Softball, Basketball, Golf, Dodge ball	4.5
3. Play on playground, chase/tag, climb trees	3.5
4. Jump rope, hopscotch, Trampoline, Bounce house	8
5. Football, Soccer, Hockey, Tennis, Kickball	7
6. Martial arts (karate, judo, etc.)	4
7. ATV, dirt bike	5
8. Dance, cheerleading, gymnastics	4
9. Swimming	4

Our results, about gender and age differences in asthma and obesity, are supported by two studies, at least, which showed that asthmatic children do more physical activities than non asthmatic children [13,18]. Also, girls are less moderately to vigorously active than boys ($p < .001$) [1]. These findings are also underpinned by older girls' higher risk of developing asthma, which could hinder them from being physically active [4]. Moreover, children after age of 6 years tend to have higher BMI [10]. Additionally, there are some studies that found asthma and obesity in general to have no significant impact on children's physical activity [9,25]. In addition, Belcher et al.'s study revealed that children between 6 and 11 years are significantly more moderately to vigorously active than those children between 12 and 14 years ($p < .001$) [1].

Significance of this study finding is that asthmatic young children who see their doctors in POC could be more adherent to their physicians' advice about increasing their physical activities, in comparison to older asthmatic children. Well controlled asthma patients may have normal lives and they are recommended to increase their exercise to decrease their weights or to keep their weights within the normal range to avoid asthma exacerbations [27]. As a matter of fact, if a student's asthma is under well controlled, s/he can participate fully in any physical activity most of the time. Furthermore, there are many famous athletes who have had asthma and have succeeded because they followed their asthma action plans [26]. Moreover, Lang et al. concluded that children whose parents

believed exercise may alleviate their asthma symptoms tended to be highly active [13].

Our exclusion of sedentary activities aimed to focus on those activities that can be easily noticed and not be over-estimated or under-estimated and affect children's weights or inducing asthma. This hypothesis is supported by other studies which excluded low-MET activities, such as watching TV because they found that those activities contribute disproportionately to the total METs, which cause them to limit their consideration to activities which would obviously increase deep inspirations [18].

This study has a number of strengths. First, this was the first study up to our knowledge explored the shared impact of asthma and obesity on children's physical activities. There are many studies have studied either of those effect on children activities. However, we think, it is difficult to separate between asthma and obesity in the clinical setting and getting recommendation for asthmatics or obese children after controlling the other factor may not practical enough when it comes to talk with the parents about the best regimens for their children. Second, we studied the effect of asthma alone, obesity alone, and their shared effect on our participants and impact of age and gender on children moderate to vigorous physical activities. Third, most of the reviewed studies results showed that asthmatic or obese children tend to have lower levels of physical activities. However, the tools that are used to measure the physical activities are not detailed as ours. For instance, the Glazebrook's study asked the children to "rate a range of activities, both active and sedentary, on a 3-point scale (none, a little, or a lot) at 3 time points in the previous 24 hours (today before school, yesterday after school, and yesterday during school)" [9]. Scores were added together to give a total score for both kinds of activities and higher scores indicating higher activity [5,9,25]. In comparison, the questionnaire used in this study examined the entire week of activities and the duration of time on average. The MET scores of the moderate and vigorous activities were then calculated only to exclude the sedentary ones such watching TV or doing home work which could be exaggerated by some parents and underestimated by others. For that purpose we used the CDC and ACSM guidelines for the definition of the activities, 3-6 METs are moderate and greater than 6 METs are vigorous. Fourth strength was that most of the reviewed studied depended only self-report questionnaire to assess the severity of asthma which could be subjected to recall bias. On the other hand, our study used both self-report questionnaire [5,25] and lung function test to evaluate the severity of asthma which gives more strength to this study.

Limitations: First, this study was a cross sectional retrospective study. Second, selection bias because all participants have been recruited from the outpatients

clinic. We expect that those patients have medical insurance, better socioeconomic status, and high educational parents' statuses, so they are more committed to the doctors' recommendations regarding encouraging their children to increase their physical activities in order to lose weight and improve their respiratory symptoms especially in advanced stage, moderate to severe asthma and high BMI%. Third constrain was the low number of participants who filled the physical activity form 75 children (55%). Further research should be prospective and try to recruit participants from the whole community to reflect the real situation of physical activities of asthmatic and non-asthmatic children.

All in all, mild and severe asthmatic young children are more physically active than the mild and severe asthmatic older children. The established declines in the physical activity are more prevalent among the asthmatic children in this sample. Regardless of their asthma diagnosis, girls were less physically active than boys, in general.

The main implication of this study is to bring clinicians' attention to focus on the children who are less physically active. These findings provide additional evidence for working with older asthmatic children and girls as they age to improve their physical activity. Clinicians may wish to encourage these particular groups to be more active and inform them about the benefits of physical activities on the asthma symptoms and the health in general. Through clear understanding of the relationship between physical activity and asthma, weight status, age, and gender, this study may provide some guidelines for future intervention to target the most vulnerable groups in a way that can improve their current health statuses through designing a multidimensional view of different points available for intervention (e.g., behavior programs, medical intervention). Also, these results provide an opportunity to offer the building blocks parents could use to ensure their children maintain a healthy weight, gain the proper nutrients, and engage in activity that will reduce their risks of health problems as adults.

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GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY

Volume 15 Issue 1 Version 1.0 Year 2015

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Risk of Inter-Related Health Issues among Children with ASD in Bangladesh

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Abstract- In recent time, autism has become a major concern, globally. Due to its rapid growth, the healthcare professionals and medical researchers have been relentlessly working to identify the causes of ASD (Autism Spectrum Disorder); though the reasons are still unclear. In light of the contemporary research paradigm on ASD, the inter-related health issues of ASD also have raised significant concerns in the field. It is very recent that the researchers are interested in the dimensions and dynamics of inter-related health issues among people with ASD. Keeping in mind the global research advancements, this empirical research focuses on exploring and examining inter-related health issues among the children with autism in Bangladesh. The results of this research clearly show that there is evidence of various forms of inter-related health issues among the children with autism in Bangladesh.

Keywords: *autism, autism spectrum disorder, ASD, inter-related health issues and autism.*

GJMR-K Classification: *NLMC Code: WY 108*



Strictly as per the compliance and regulations of:



Risk of Inter-Related Health Issues among Children with ASD in Bangladesh

Dr. Samiul Parvez Ahmed ^α & Mahmuda Shahzabeen Ahmed ^σ

Abstract- In recent time, autism has become a major concern, globally. Due to its rapid growth, the healthcare professionals and medical researchers have been relentlessly working to identify the causes of ASD (Autism Spectrum Disorder); though the reasons are still unclear. In light of the contemporary research paradigm on ASD, the inter-related health issues of ASD also have raised significant concerns in the field. It is very recent that the researchers are interested in the dimensions and dynamics of inter-related health issues among people with ASD. Keeping in mind the global research advancements, this empirical research focuses on exploring and examining inter-related health issues among the children with autism in Bangladesh. The results of this research clearly show that there is evidence of various forms of inter-related health issues among the children with autism in Bangladesh.

Keywords: autism, autism spectrum disorder, ASD, inter-related health issues and autism.

I. INTRODUCTION

In recent time, autism has become a major concern, globally. To be more specific, “...it is the fastest growing serious developmental disability and since 2002 through 2006 its growth rate is around 57 per cent” (Autism Speaks, 2011)¹. Though the rate of autism is increasing to a greater extent, the reasons/causes behind autism haven't been identified clearly (Trotter et al. 1999). Several arguments can be observed regarding causes of autism (e.g. hereditary, environmental factors, genetics) but, none of them is conclusive and their claim is often disproportionate (e.g. some issues are overstated and some are understated) (Hallmayer et al. 2011). Some also argue that there is link between autism and childhood vaccination, though there is no scientific proof for this claim (Freitag, 2007). Irrespective of the causes of autism, it is for real that the autistic people suffer a lot of problems in terms of various forms of physical and mental issues and, thus, one of the primary concerns is to identify the common problems that the autistic people face and how to treat them.

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II. AUTISM: CONCEPT AND RELEVANT ISSUES

It is difficult to define autism with a single universally accepted definition. Medical professionals and relevant academics/researchers hold vast range of concepts regarding autism. Firstly, autism, rather than a well-defined medical condition, it is considered as a “spectrum of disorders” that ranges from biological dysfunctions to psychological disorders. Hence, from technical perspective, autism can be defined as a “...behavioural syndrome of multiple neurological injuries associated with a wide variety of medical conditions” (Gillberg, 1990). In more non-technical words it can be defined as “...a spectrum of behavioral anomalies characterized by impaired social interaction and communication, often accompanied by repetitive and stereotyped behavior” (Ashwood and Water, 2004). It means that, in broader sense, autism affects a person's overall social skills – speech competencies, encoding and decoding language skills, socio-relational skills and overall socio-communicative skills. Though the major focus is always given to the psychological aspects while defining autism, its biological anomalies cannot be ignored. In some cases severe biological anomalies (e.g. inadequate motor skills, tics issues, hearing and vision issues) can even make an autistic person physically disable. In short, it can be said that the “fundamental problems” that directly results from autism are broadly various forms of mental problems (e.g. social and learning problem); physical problems (e.g. lack of motor skills, feeding and eating problem); and behavioural problems (e.g. repetitive patterns of behaviour problem).

a) Contemporary Issues

Currently, it is widely argued that children with Autism Spectrum Disorder (ASD) prone to experience “other inter-related”, both mental and physical, health issues than that of the core “fundamental problems” (as mentioned in the previous section). In recent time, a researcher of health psychology and a clinical child psychologist, University of Missouri, USA, Micah Mazurek, argued that adolescents with ASD also have chronic gastrointestinal problems, such as constipation, abdominal pain, bloating or nausea (Saracino, 2012). In line with this argument, a recent study conducted by her found that many children with autism also experience anxiety, chronic gastrointestinal (GI) problems and atypical sensory responses, which are heightened

¹ It is estimated that 1% of the world's population or 67 million are affected by autism (Autism Speaks, 2011).

reactions to light, sound or particular textures (McIntyre, 2012). Another study found that children with autism have sleeping disorder (Mayes, Calhoun, 2009). Similarly, various health organizations state that autism often associated with other inter-related health specific issues, such as, epilepsy, dental issues, tics and other mental issues².

Therefore, the main objective of this research paper is to examine and discuss a range of inter-related health problems of autism and, subsequently, explore inter-related health problems among autistic people, particularly among the autistic children, in the Bangladeshi context.

III. AUTISM AND OTHER INTER-RELATED HEALTH ISSUES

As mentioned earlier, it is often argued that the autism may associated with various interrelated health problems which, based on their nature, can be categorized into physical and mental issues.

a) *Prevalence of Physical Issues among ASD*

i. *Sleeping disorder*

One of the concerns regarding health issues among ASD children is that they often suffer from various forms of sleeping disorders (Mayes and Calhoun, 2009). According to a study conducted by Mayes and Calhoun (2009) with 477 autistic children, it was found that, in most of the cases, the children not only suffer from sleeping disorders, but also this tendency increases as the level of the severity of ASD increases. According to another study, children with ASD sleep less (e.g. insomnia) than their typical peers (Rudy, 2009a).

b) *Poor nutrition due to Food Selectivity & other Feeding Problems*

According Matson and Fodstat (2009), "food selectivity and other feeding problems are endemic in children with autism spectrum disorders (ASD)". To be more specific, the authors stated that autistic children, due to their food selectivity issue, often suffer from poor nutrition. Moreover, in many cases, autistic children with food selectivity problem show aggression in refusing food.

c) *Anxiety, Sensory Over-Responsivity and Gastrointestinal Problems*

It is known that in many cases children with autism spectrum disorders (ASD) suffers from Anxiety, Sensory Over-Responsivity and Gastrointestinal Problems (Mazurek et. al., 2013; Rudy, 2009b, Molly, 2003). However, a recent study (conducted in 2013)

points out that these variables haven't been examined before in light of their association within themselves and, thus, the study revealed their degree and nature of association (Mazurek et. al., 2013). According to the study—

"...twenty-four percent of the sample experienced at least one type of chronic GI problem (constipation, abdominal pain, bloating, diarrhea, and/or nausea lasting three or more months). Children with each type of GI problem had significantly higher rates of both anxiety and sensory over-responsivity. Sensory over-responsivity and anxiety were highly associated, and each provided unique contributions to the prediction of chronic GI problems in logistic regression analyses. The results indicate that anxiety, sensory over-responsivity and GI problems are possibly interrelated phenomenon for children with ASD, and may have common underlying mechanisms" (Mazurek et. al., 2013:165).

d) *Epilepsy & Autism*

In Australia, it is estimated that around thirty percent of people with ASD develop epilepsy (Autism Help)³. According to Autism Help—"Children with a severe intellectual disability are most likely to have seizures. Seizures most often develop during early childhood, with puberty being the next peak onset time, however onset can occur at any age".

e) *Sexuality & Autism*

It is argued that many people with ASD become sexually active, but often do not understand the consequences (Autism Help). In many cases, though the autistic people become sexually active (biologically), but these people lack maturity and social skills to properly deal with sexual skills.

f) *Dental Issues*

Autistic children often suffer from poor dental health (Autism Help). They usually have high level of tolerance for any kind of pain and, hence, when they suffer from dental pain it is difficult to notice their problems. Behavioural differences/changes may be taken as indications of their problems.

g) *Prevalence of Mental Issues among ASD*

It is obvious that the Autistic children have mental issues; however, they often victim of other inter-related mental problems which results from their lack of integration to their social surroundings or to their normal counter peer groups. The common problems that they face are low self-esteem, depression and various forms of anxieties (Autism Help).

² Source: Autism Help: A health organization that work in the Autism area known as Gateway Support Services, Australia. <http://www.autismhelp.info/default.aspx>

³ Source: Autism Help: A health organization that work in the Autism area known as Gateway Support Services, Australia. <http://www.autismhelp.info/default.aspx>

IV. EMPIRICAL STUDY

a) *Background of the Empirical Study: Autism & Inter-Related Health Issues in Bangladesh*

In Bangladesh, there are no exact statistics on how many children is experiencing autism (Hossain, 2011). However, Ranjit Kumar Biswas, secretary to Social Welfare Ministry, claims that about 10% of the country's people could be challenged where 1% to be affected by ASD⁴. Moreover, till now, in Bangladesh, we do not have sufficient data (secondary data) or research work regarding prevalence of other health related issues among children having ASD. Therefore, the purpose of this research paper is to explore other health related issues among children with ASD in Bangladesh based on primary data.

b) *Methodology*

i. *Central Research Question*

Do autistic children suffer from inter-related health problems?

ii. *Objective*

The objective of this report is to explore whether autistic children suffer from inter-related health problems or not, and, subsequently, their implications among autistic children of the Bangladesh.

iii. *Hypothesis*

Six particular alleged inter-related health problems (as discussed in the literature review section) among children with ASD are considered in this study; they are sleeping disorder, constipation, stomach pain, gastrointestinal problem, obesity, and epilepsy. Thus, six sub-hypothesis were tested in order to answer the central question:

Association of ASD and Sleeping Disorder

H₀: ASD is not associated with sleeping disorder

H₁: ASD is associated with sleeping disorder

Association of ASD and Constipation

H₀: ASD is not associated with constipation

H₁: ASD is associated with constipation

Association of ASD and Stomach Pain

H₀: ASD is not associated with stomach pain

H₁: ASD is associated with stomach pain

Association of ASD and Gastrotestinal Issue

H₀: ASD is not associated with gastrotestinal issue

H₁: ASD is associated with gastrotestinal issue

Association of ASD and Obesity

H₀: ASD is not associated with Obesity

H₁: ASD is associated with Obesity

Association of ASD and Epilepsy

H₀: ASD is not associated with Epilepsy

H₁: ASD is associated with Epilepsy

iv. *Research Approach*

Considering the scope and resource, a case study approach was followed. As a case, one particular centre/institute that deals with autism was considered as "case subject"; and the autistic children that are registered in that centre were considered as "research elements". In order to compare the prevalence of the alleged inter-related health issued among children with ASD, a group of non-autistic children (children who do not have ASD) were considered as "comparison group" in the study.

v. *Case Subject*

Beautiful Mind (A Special Centre for Autistic & Mentally Challenged Children), Uttara, Dhaka, Bangladesh.

vi. *Research Elements (Autistic Children)*

The registered autistic children at Beautiful Mind, Uttara, Dhaka, Bangladesh.

vii. *Comparison Group (non-Autistic Children)*

Children who are enrolled in various mainstream education institutes and who do not have ASD.

viii. *Sample Size*

50 children with ASD and 25 ordinary (non-autistic) children.

ix. *Sampling Technique*

Total population of the case subject (Beautiful Mind) was considered for the study. Total population was approached for the study; however, parents of 50 children with ASD of the institute participated in the study. For the "comparison group", convenient sampling was used. The questionnaire was developed in such a way that it is self explanatory and thus the questionnaires were distributed among the parents, who agreed to participate in the study. Subsequently, the respondents returned the completed questionnaires afterwards. The parents were given the flexibility to consult the researcher in case they are not clear about any aspect of the questionnaire.

x. *Data Collection Tool*

Semi-Structured Questionnaire.

xi. *Ethical Consideration*

As the subject of the study (children) are minor, their parents and/guardians were considered as respondents for this study. Moreover, due to privacy protection issue, anonymity of the respondents is ensured throughout the research.

xii. *Testing Hypothesis*

Chi-square test is performed to test the hypothesis.

⁴ The Daily Star, Sunday, July 24, 2011. Source: <http://archive.thedailystar.net/newDesign/news-details.php?nid=195486>

V. RESULTS & DISCUSSIONS

a) *Overview of the Case-Subject: Beautiful Mind*

Beautiful Mind is a private organization registered under the Ministry of Social Welfare, Bangladesh. The center is situated at Dolipara North of Uttara Model Town, Dhaka. The area is in a semi-rural with urban development closing in around the center. This centre was established in July 2004 by the founder chairperson Dr. Shamim Matin Chowdhury – a child and adolescence psychiatrist and an autism specialist in Bangladesh. Since then the centre is offering wide range of flexible programs for autistic and mentally challenged children. The centre responds specific needs of each individual depending on their issues. The student population of special needs comes from varied socio economic and cultural backgrounds with no apparent majority group. The centre has modern equipped physiotherapy, speech-therapy and occupational-therapy laboratories to support children's clinical needs. Academically this centre follows the National Curriculum and the Foundation Stage but modified by centre staff to meet the needs of pupils with autism and mental retardation. Moreover special approaches are followed to teach the special children, such as Verbal Prompt, TEACCH, PECS and ABA system are used to provide individualized methodology for each pupil.⁵

b) *Data Analysis and Findings*

In relation to the earlier discussion regarding autism and inter-related health issues, the primary data of the autistic children of the Beautiful Mind also shows that there is prevalence of some inter-related health issues among the autistic children (see figure 1).

i. *Sleeping Disorder*

64% of the respondents highlighted the fact that their children have sleeping disorder, though the nature of the problems varies among the children. The major issues are: (i) less sleeping hours compare to normal sleeping standards; (ii) difficulty in sleeping normally (medication needed); (iii) if sleeps few hours at day time, do not sleep at night. In few cases, the problem is quite serious; for instance, one of the respondents stated that:

"...Yes, he has various issues with his sleeping. Firstly, he has sleeping disorder. He doesn't have deep sleep. A slight sound wakes him up. Moreover, he doesn't sleep at all at night if there are any irregularities with his medications" (Interview: respondent code: 15)

⁵ Source: Beautiful Mind Website: <http://www.beautifulmindbd.net/>

Figure 1. Inter-related Health Problems among Children with ASD in Bangladesh

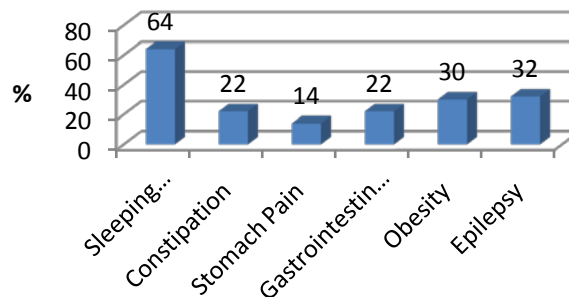


Figure 1 : Inter-related Health Problems among Children with ASD in Bangladesh

ii. Constipation

Around 22% respondents said that their children have constipation problem. Most of them said that their children do not want to eat fruits and vegetables. They prefer to eat chips, crisps and unhealthy fast food. So they suffer from constipation.

iii. Stomach Pain

According to the primary data, 14% respondents said that their children suffer from stomach pain. Some said that though their children cannot speak clearly but they could communicate through other means of communications to make them understand that they have stomach pain.

iv. Gastrointestinal Problem

Around 22% parents said that their children are suffering from Gastrointestinal problem. Some said that their children seriously suffer from gastric. Some said that they suffer occasionally.

v. Obesity

30% patients are obese. Some mother said that their children eat a lot. They do not understand that whether their stomachs are full or not. That might be the reason that these children suffer from obesity.

vi. Epilepsy

According to the data we can see that 32% children are suffering from epilepsy. One of the respondents said that, "when my child suffers from fever then he suffers from epilepsy". Most of the patients are under medication for epilepsy.

The above discussion is descriptive and that does not signify the statistical relationships of the concerned inter-related health issues and ASD. Thus, in order to answer the central question of the study, hypothesis testing is conducted in the following section.

c) Hypothesis Tests

Table 1 : Prevalence of Sleeping Disorder among ASD and Non-ASD Children

	Positive Sleeping Disorder	Sleeping Disorder Negative	Total
ASD	32	18	50
Non-ASD	1	24	25
Total	33	42	75

Chi-square value

24.35; Result: Failed to accept null hypothesis; ($\alpha=0.05$; $df=1$).

Decision

Evidence support that ASD may be associated sleeping disorder.

Table 2 : Prevalence of Constipation among ASD and Non-ASD Children

	Positive Constipation	Constipation Negative	Total
ASD	11	39	50
Non-ASD	0	25	25
Total	11	64	75

Chi-square value

6.45; Result: Failed to accept null hypothesis; ($\alpha=0.05$; $df=1$).

Decision

Evidence support that ASD may be associated with constipation.

Table 3: Prevalence of Stomach Pain among ASD and Non-ASD Children

	Positive Stomach Pain	Stomach Pain Negative	Total
ASD	7	43	50
Non-ASD	2	23	25
Total	9	66	75

Chi-square value

0.57; Result: Null hypothesis cannot be rejected; ($\alpha=0.05$; $df=1$)

Decision

Evidence does not support that ASD and stomach pains are associated

Table 4: Prevalence of Gastrotestinal problem among ASD and Non-ASD Children

	Positive Gastrotestinal Problems	Gastrotestinal Problem Negative	Total
ASD	11	39	50
Non-ASD	4	21	25
Total	15	60	75

Chi-square value

0.38; Result: Null hypothesis cannot be rejected; ($\alpha=0.05$; $df=1$)

Decision

Evidence does not support that ASD and gastrotestinal problems are associated

Table 5: Prevalence of Obesity among ASD and Non-ASD Children

	Positive Obesity	Obesity N/A	Total
ASD	15	35	50
Non-ASD	7	18	25
Total	22	53	75

Chi-square value

0.03; Result: Null hypothesis cannot be rejected; ($\alpha=0.05$; $df=1$)

Decision

Evidence does not support that ASD and obesity are associated

Table 6: Prevalence of Epilepsy among ASD and Non-ASD Children

	Positive Epilepsy	Epilepsy N/A	Total
ASD	16	34	50
Non-ASD	0	25	25
Total	16	59	75

Chi-square value

10.17; Result: Failed to accept null hypothesis; ($\alpha=0.05$; $df=1$)

Decision

Evidence support that ASD may be associated epilepsy.

The above results show that, statistically ASD does have association with sleeping disorder, constipation and epilepsy. This findings support the argument that children with ASD are prone to experience other inter-related health issues. However, it is to be noted that the results for other factors (stomach pain, obesity and gastrotestinal issues) do not support this argument.

VI. TREATMENT

An Autistic child is a big problem for a family. Not only the autism but also the interrelated health issues have a negative effect for the patient. The inter-related health issues can critically influence the regular life of a person subject to autism and moreover these issues can have significant effects on their functioning at home and in school.

Clinicians should be aware that anxiety, GI problems and sensory sensitivity often co-occur in individuals with ASD. Effectively managing these concurrent issues may improve children's quality of life and their responses to treatment. Parents need to be aware that these problems may underlie some of their children's difficulties, so if they notice any symptoms, they should talk to their doctors or therapist about treatment options (Mazurek et al. 2013).

It is not possible to cure autism with any type of medication. But the associated health issues like anxiety, aggressive behaviour, sleeping disorder, epilepsy can be controlled with medication. Parents and doctors should be careful about medications; because all medications have short term or long term side effects. The side effects that occur from medications are- weight gain, nausea, sleepiness, increased aggression, headaches and long term liver or kidney problem. So parents and doctors should be very careful to use medicines for autistic children.

VII. CONCLUSION

The health care services regarding autism and standard of diagnosis in this field in our country is still very basic (Ethirajan, 2011). Moreover, it is quite unfortunate that there is a dearth of nationwide statistical data in this field⁶. It is good that in 2001 Bangladesh government passed Disability Act and, in addition, the Government established the 'Centre for Neurodevelopment and Autism in Children' at the Bangabandhu Sheikh Mujib Medical University (Autism Speaks⁷). It is true that the awareness regarding autism is increasing but the current health services mainly focus

⁶ Bangladesh does not have specific data on those affected by autism but officials estimate that around 150,000 children may be classified as autistic (Ethirajan, 2011).

⁷ <http://www.autismspeaks.org/site-wide/bangladesh>

on the fundamental issues of autism in our country. There is not much concern regarding the inter-related health issues among the autistic people among the health professionals in this field. But this study clearly shows that there is evidence of various forms of inter-related health issues among the children with autism in Bangladesh. Thus, along with all other critical issues of autism, the inter-related health issues of autism should be brought into the limelight of contemporary autism research and these issues should be addressed through the local autism health care facilities.

VIII. ACKNOWLEDGEMENT

Special thanks to Dr. Shamim Matin Chowdhury, founder chairperson of the Beautiful Mind, for providing invaluable remarks for our research.

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GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY

Volume 15 Issue 1 Version 1.0 Year 2015

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Semiparametric Estimation of AUC from Generalized Linear Mixed Model

By Okeh UM & Oyeka ICA

Ebonyi State University, Nigeria

Abstract- Methods of evaluating the performance of diagnostic tests are of increasing importance in medical science. When a test is based on an observed variable that lies on a continuous scale, an assessment of the overall value of the test can be made through the use of a Receiver Operating Characteristic (ROC) curve. The ROC curve describes the discrimination ability of a diagnosis test for the diseased subjects from the non-diseased subjects. The area under the ROC curve (AUC) represents the probability that a randomly chosen diseased subject will have higher probability of having disease than a randomly chosen non-diseased subject. Semi-parametric being a ROC curve estimation method is widely used in making inferences from diagnostic test results that are at least measurements on ordinal scale. In this paper, we proposed a method of semi-parametric estimation in which predicted probabilities of discordant pairs of observation are obtained from generalized linear mixed model (GLMM) and used in modeling ROC and AUC. The AUC obtained which is time dependent is equivalent to the Mann-Whitney statistic (Hanley and McNeil, 1982) often applied for comparing distributions of values from the two samples.

Keywords: AUC, ROC, GLMM, GDM, semi-parametric, mann-whitney.

GJMR-K Classification: NLMC Code: QZ 241



SEMI-PARAMETRIC ESTIMATION OF AUC FROM GENERALIZED LINEAR MIXED MODEL

Strictly as per the compliance and regulations of:



Semiparametric Estimation of AUC from Generalized Linear Mixed Model

Okeh UM ^α & Oyeka ICA ^σ

Abstract- Methods of evaluating the performance of diagnostic tests are of increasing importance in medical science. When a test is based on an observed variable that lies on a continuous scale, an assessment of the overall value of the test can be made through the use of a Receiver Operating Characteristic (ROC) curve. The ROC curve describes the discrimination ability of a diagnosis test for the diseased subjects from the non-diseased subjects. The area under the ROC curve (AUC) represents the probability that a randomly chosen diseased subject will have higher probability of having disease than a randomly chosen non-diseased subject. Semi-parametric being a ROC curve estimation method is widely used in making inferences from diagnostic test results that are at least measurements on ordinal scale. In this paper, we proposed a method of semi-parametric estimation in which predicted probabilities of discordant pairs of observation are obtained from generalized linear mixed model (GLMM) and used in modeling ROC and AUC. The AUC obtained which is time dependent is equivalent to the Mann-Whitney statistic (Hanley and McNeil, 1982) often applied for comparing distributions of values from the two samples. The proposed methods are illustrated using data on women at risk for gestational diabetes mellitus. Result indicates that varying cutoff values for screening pregnant women exists for different time period while an optimal cutoff value is recommended for screening all women at risk for GDM given that the procedure yielded smooth ROC curves. The predicted probabilities obtained from GLMM method has a high statistical efficiency since for all the trimesters, there exists statistical significance. This study therefore demonstrated that the semi parametric GLMM method provided reliable, unbiased, and consistent estimates for the

parameters while the AUCs are all statistically significant. The computations are supported by SAS version 9.0.

Keywords: AUC, ROC, GLMM, GDM, semi-parametric, mann-whitney.

I. INTRODUCTION

In health studies, the diagnosis of a patient are very often based on some classification errors calibrated based on the sensitivity and specificity. An individual presenting for a screening test for a disease, is discriminated based on a cut-off value c whether he/she is healthy or diseased when test results are measurements on at least the ordinal scale. Many procedures exist for estimating the accuracy of test measurements such as the parametric, nonparametric and semi-parametric methods and their associated summary measures. In this paper, we will propose a semi-parametric regression type method of obtaining predicted probabilities from the Generalized Linear Mixed Model (GLMM) and using them to model the receiver operating characteristic (ROC) curve and area under the ROC curve (AUC) for continuous binary test results that are time dependent.

Suppose Y and X denotes the test result of subjects with and without disease respectively. Let c be cut-off value. Then $P(X > c) = G(c)$ and $P(Y > c) = F(c)$ where $F(c)$ is sensitivity and $1-G(c)$ represents specificity. Therefore ROC is a plot of $F(c)$ versus $G(c)$ for all possible thresholds, c . In terms of TPR and FPR at c ,

$$ROC(.) = \{(FPR(c), TPR(c)), c \in (-\infty, \infty)\} \quad (1)$$

The accuracy of ROC is summarized by the AUC given as

$$AUC = P(X > Y) = \int_0^1 ROC(t) dt. \quad (2)$$

This is the probability that a randomly chosen diseased subject will have higher probability of having disease than a randomly chosen non-diseased subject.

Since different estimation methods can provide a span of estimated AUC values on the same data set,

their properties are always examined in order to provide a recommendation as to the preferred approach.

Dorfman and Alf (1969) proposed a parametric iterative method for obtaining the maximum likelihood estimates of the parameters of a bi-normal ROC curve to model ordinal data. They assumed that test results for the diseased (X) and non-diseased (Y) populations are normally distributed respectively as

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$$X \sim N(\mu_X, \sigma_X^2) \text{ and } Y \sim N(\mu_Y, \sigma_Y^2). \quad (3)$$

While parametric binormal ROC curve is given as

$$ROC(t) = \Phi(a + b\Phi^{-1}(t)), 0 \leq t \leq 1, \quad (4)$$

$$\text{where } a = \frac{\mu_X - \mu_Y}{\sigma_X}, b = \frac{\sigma_Y}{\sigma_X}. \quad (5)$$

Here a and b are parameter estimates which gives the statistical inference while Φ denotes the standard normal cumulative distribution function. By algebraic simplification, the AUC is given as:

$$AUC = \Phi \left(\frac{(\mu_X - \mu_Y)}{\sqrt{\sigma_X^2 + \sigma_Y^2}} \right) = \Phi \left(\frac{a}{\sqrt{1 + b^2}} \right) \quad (6)$$

Reiser and Faraggi(2002) and Goddard and Hinberg (1990) proposed the transformation (say logarithmically) of test results and making it normal due to the violation of the normality assumption. They proposed the transformed normal (TN) approach which is a parametric estimation method based on the normal theory. It involves applying a Box-Cox power transformation (Box and Cox,1964) to the data and subsequently using the N estimator to the transformed data.

In general, the problems identified with maximum likelihood method of estimating parameters in parametric method is the inability of the parameter

estimates to quickly attain convergence because it is an of iterative method. There exists also the restrictive assumptions of normality or transformation to normality of the parametric method about the distribution of test results making the estimates inconsistent thereby giving a misleading picture of the regression relationship when the assumption is violated (Pepe,2003).

According to Hanley and McNeil (1982), the empirical non-parametric method uses the MW statistic in estimating ROC curves. As usual, they are used when the normality assumption for test results is violated. Here AUC is calculated using the MW version of the two-sample rank-sum statistic of Wilcoxon as

$$A\hat{U}C = \frac{1}{n_1 n_0} \sum_{i=1}^{n_1} \sum_{j=1}^{n_0} \Omega(Y_i^+, Y_j^-) \quad (7)$$

$$\text{where } \Omega(Y_i^+, Y_j^-) = \begin{cases} 1 & \text{if } Y_i^+ > Y_j^- \\ \frac{1}{2} & \text{if } Y_i^+ = Y_j^- \\ 0 & \text{if } Y_i^+ < Y_j^- \end{cases} \quad (8)$$

Where n_1 and n_0 are number of subjects that are diseased and non-diseased respectively.

Y_i^+ while is the i th diagnostic test results for the diseased individuals and Y_j^- is the j th diagnostic test results for the non-diseased individuals. The AUC just

like the MW statistic is suitable for comparing two populations (n_1 and n_0) by taking covariate effects into account. Equation 8 provides an unbiased estimate given as.

$$P(Y_i^+ > Y_j^-) + \frac{1}{2} P(Y_j^- = Y_i^+) \quad (9)$$

Therefore

$$A\hat{U}C = \frac{1}{n_1 n_0} \sum_{i=1}^{n_1} \sum_{j=1}^{n_0} P(Y_i^+ > Y_j^-) + \frac{1}{2} P(Y_j^- = Y_i^+) \quad (10)$$

In general, nonparametric estimation method does not yield smooth curve, especially in small samples (Zou et al, 1998). They models avoid restrictive assumptions of the functional form of the regression function. There is also lack of a one to one correspondence between TPR and FPR values makes inference awkward (Zou et al, 1998).

Dodd and Pepe (2003) proposed a semi-parametric AUC regression model for data with a non-normally distributed response variable which can adjust for continuous and discrete covariates. Assume that one needs to adjust the AUC for a covariate X , the covariate-specific AUC can be expressed as

$$AUC_{ij} = P(Y_i^D > Y_j^{\bar{D}} | X_i, X_j) \quad (11)$$

Where i is the i th response in diseased (or treatment) group with covariate value X_i and j is the j th response in non-diseased (or control) group with

covariate value X_j . Often one is interested in estimating the AUC at a specified covariate level, i.e.

$$P(Y_i^D > Y_j^{\bar{D}} | X_i = X_j = X). \quad (12)$$

Dodd and Pepe applied this model to the GLM framework which allows one to model the AUC with covariates, in which case their model can be written as,

$$g(AUC_{ij}) = X_{ij}^T \beta, \quad (13)$$

where g is a monotone link function such as the probit or logit link, X_{ij} is a vector function of

X_i and X_j and β is a vector fixed and unknown parameters to be estimated. Note that

$$E(I(Y_i^D > Y_j^{\bar{D}}) | X_{ij}) = AUC_{ij}. \quad (14)$$

Thus, for estimating the parameters in the model, Dodd and Pepe proposed the use of the logistic regression model where the response variable is a

Bernoulli variable. Dodd and Pepe demonstrated that the estimates of parameters are found as solution to the usual score equations given by

$$\sum_i^{N_D} \sum_j^{N_{\bar{D}}} \frac{(I_{ij} - AUC_{ij})}{V(I_{ij})} \frac{\partial AUC_{ij}}{\partial \beta}, \quad (15)$$

Where $I_{ij} = I(Y_i^D > Y_j^{\bar{D}})$. Therefore, one obtains this estimate using standard statistical software.

According to Colak et al (2012) as well as Wolfgang et al(2004), the most preferred method of estimation is the semi-parametric method because it combines the flexibility of the nonparametric method with the advantages accruable to the parametric procedure in achieving better results. Semi-parametric (SP) approach is an intermediate strategy between

parametric and non-parametric methods for estimating the ROC curve in the sense that it assumes a parametric bi-normal form for the ROC curve, but does not assume that the diagnostic test results follow any particular distribution. This informed the choice of the method in this work.

II. LINEAR REGRESSION MODEL

A linear regression model by matrix notation is given as:

$$\underline{Y} = \underline{X} \underline{\beta} + \underline{\varepsilon} \quad (16)$$

Where $\underline{Y} = n \times 1$ is a column vector of observations, $X = n \times (p+1)$ is a design matrix of regressors, $\underline{\beta} = p \times 1$ is a column vector of regression coefficients and $\varepsilon = n \times 1$ is a column vector of error term which is independent and identically distributed such that $\varepsilon(0, \sigma^2 I)$. Note that for linear regression model, $E(Y) = X\underline{\beta}$ is actually the expected probability

$$\underline{\hat{\beta}} = (X'X)^{-1} X'Y \quad (17)$$

Where $\underline{\hat{\beta}} \sim N(\underline{\beta}, (X'X)^{-1} \sigma^2)$ and $(X'X)^{-1}$ is the inverse of the nonsingular variance-covariance matrix.

that on the average a randomly selected subject from the population test or respond positive to the condition under study while the variance is given as $\sigma^2 I$, where I is an $n \times n$ identity matrix. The estimation of β can be carried out using the least square method by obtaining $\hat{\beta}$ as the best estimate of β through the minimization of the sum of squared errors. The result is

III. GENERALIZED LINEAR MODEL (GLM)

GLM is an extension of the linear regression model and for modeling binary data, GLM is made up of a linear predictor given as

$$\eta = X\beta \quad (18)$$

And inverse link function (g^{-1}) which describes how the mean, $E(Y) = \mu$ depends on the linear

predictor thus converting a linear predictor into a mean. It is given as

$$g^{-1}(\eta) = \mu \quad (19)$$

This link function a smooth and invertible linearizing function which transforms the expectation of the response variable to the linear predictor. The third

component of GLM is a variance function that describes how the variance, depends on the mean and it is

$$Va(rY) = V(g^{-1}(X\beta)) = V(g^{-1}(\eta)) \quad (20)$$

Meanwhile, GLMM is a model extension of GLM in which the linear predictor contains both fixed effects

and random effects (McCullagh and Nelder, 1989). In matrix notation, it is given as

$$Y = \eta + \varepsilon = X\beta + Zu + \varepsilon \quad (21)$$

where

$$u \sim N(0, G); \varepsilon \sim N(0, R); E(u, \varepsilon) = 0; Cov(\varepsilon, u) = 0.$$

As defined previously for Y , β is a $p \times 1$ column vector of fixed effects, u is a $q \times 1$ vector of random effects, ε is a $n \times 1$ vector of random error terms, X is the $n \times p$ design matrix for the fixed effects relating to β , Z is the $n \times q$ design matrix for the random effects relating to

u . The structure of the covariance matrices of G and R specifies the structure of correlation among the random effects and error term respectively. The variance of Y for GLMM is given as:

$$V(Y) = ZGZ' + R \quad (22)$$

Where Z is a diagonal matrix and A is a diagonal matrix that contains the variance functions of the model.

IV. THE PROPOSED METHOD

To obtain the predicted probability from GLMM, we incorporate the time of measurement of binary data

$$\ln\left(\frac{\pi_{it}}{1-\pi_{it}}\right) = \eta_{it} = X_{it}\underline{\beta} + Z_{it}\underline{u}_i \quad (23)$$

where π_{it} is the predicted probability of the positivity of i th randomly selected subject at time t for

for subjects having n observations. Since the binary logistic model is a linear relationship between the natural logarithm and the linear component. Then

$i = 1, 2, \dots, n; t = 1, 2, \dots, T$. Here T is total time period and η_{it} is the linear predictor for i th subject at time t . Simplifying equation gives

$$\hat{\pi}_{it} = \frac{e^{X_{it}\hat{\beta} + Z_{it}\hat{u}_i}}{1 + e^{X_{it}\hat{\beta} + Z_{it}\hat{u}_i}} \quad (24)$$

This estimated predicted probability results from fitting the values of the parameter estimates of

$\hat{\beta}$ and \hat{u} evaluated through the application of Henderson (1953) mixed model equations given as

$$\begin{pmatrix} X'R^{-1}X & X'R^{-1}Z \\ Z'R^{-1}X & Z'R^{-1}Z + G^{-1} \end{pmatrix} \begin{pmatrix} \beta \\ u \end{pmatrix} = \begin{pmatrix} X'RY \\ Z'RY \end{pmatrix} \quad (25)$$

These estimates are respectively obtained and the solution is given as

$$\hat{\beta} = (X'V^{-1}X)^{-1}X'V^{-1}Y, \hat{u} = GZ'V^{-1}(Y - X\hat{\beta}) \quad (26)$$

where $V = ZGZ' + R$

V. CONSTRUCTING ROC CURVE

The estimated predicted probability will then serve as a bio-marker for constructing the ROC curve for discriminating a diseased subject from a non-diseased subject longitudinally. The procedure is first to obtain estimates of sensitivity and specificity from a four-fold table so as to have insufficient pairs of sensitivity and 1-specificity that are incapable of producing the actual ROC curve analysis. To obtain sufficient pairs capable of generating the actual smooth ROC curve, a series of pairs of sensitivity and 1-specificity up to the sample size under consideration $(sn(1), 1-sp(1)), \dots, (sn(n), 1-sp(n))$ is calculated from varying cuts of positivity escalated by increments of 0.005 in predicted probability. The ROC curve is created by plotting for n number of subjects at t time, n pairs of sensitivity and 1-specificity data points starting with the strictest positive criterion of 1 to the loosest positive criterion of 0.005.

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VI. ESTIMATING AUC FROM ESTIMATED PREDICTED PROBABILITY

The AUC is given in a closed form for the purpose of this study as:

$$AUC = \int_0^1 ROC(t_{X,Z}) dt_{X,Z}, \quad (27)$$

This is the ROC value with false-positive rate t that is associated with the fixed effect predictor X and random effects predictor Z where the integration limits run from 0 to 1. Due to the difficult nature of obtaining the result as seen by other authors (Dorfman et al, 1969), we will alternatively construct AUC based on predicted

probabilities from binary measure models, by adapting the MW method to compare the size of the predicted probabilities of each discordant pair. This is achieved by dichotomizing the predicted probability so that two probabilities given as π_{it}^+ and $(1-\pi_{it}^+)$ is assumed to

represent predicted probability of the diseased and non-diseased responses for the i th subject respectively at time t for the binary measure design. The MW method is the choice because under the GLMM framework, there

is no simple closed-form solution of the ROC curve and the MW method yields ROC estimates with a good precision. Here the AUC is given as

$$AUC = \frac{1}{n_D n_{\bar{D}}} \sum_{i=1}^n \sum_{t=1}^T u_{it} \quad (28)$$

Where n_D and $n_{\bar{D}}$ are the numbers of observed values for the diseased and non-diseased subjects respectively while t and T are time of test measurement and total time period of measurement respectively.

Also u_{it} is a function comparing the test result of i th subject with and without disease at time t . The total number of (discordant pairs) sample observations, n as:

$$n = n_D + n_{\bar{D}} \quad (29)$$

The difference between the AUC given above and that suggested by other authors such as Hanley and McNeil (1982) is that here AUC is calculated from predicted probabilities that are time dependent instead of test scores. For each discordant pair, ordering of the corresponding predicted probabilities are compared in relation to the observed outcome values, and the AUC is calculated based on these ordering results so as to

compare the size of the predicted probabilities of each discordant pair. In binary measure design, where there exist complete discrimination of health status, each subject has two possible mutually exclusive outcomes either Yes (diseased coded 1) or No (non-diseased usually coded 0) whose values may vary from time to time. This is represented as

$$u_{it} = \begin{cases} 1, & \text{if } x_{it} \text{ is the test score in the } i\text{th subject screened at} \\ & \text{time } t \text{ that tested positive} \\ 0, & \text{otherwise} \end{cases} \quad (30)$$

for $i = 1, 2, \dots, n; t = 1, 2, \dots, T$

The values of 0 and 1 as outcomes of this function shows that the subjects health status are well discriminated (Bernd et al, 2003; Colak et al, 2012). Evaluation of this function through the ordering procedure gives the unbiased estimate suitable for use in calculating the AUC.

VII. ILLUSTRATIVE EXAMPLE

The data for this study were obtained from the medical record units of five randomly selected hospitals in Ebonyi State, Nigeria. The data represents binary test results of 1114 pregnant women susceptible for gestational diabetic mellitus (GDM). These are measurements taken at various time periods (trimesters).

Table 1 : Table showing screening test results and final diagnosis using OGTT by trimesters OGTT (Gold standard)

	1 st Trimester GDM present =B; GDM absent= \bar{B}			2 nd Trimester GDM present =B; GDM absent= \bar{B}			3 rd Trimester GDM present =B; GDM absent= \bar{B}			All Trimester GDM present =B; GDM absent= \bar{B}		
Test result of GCT FOR GDM	<i>B</i>	\bar{B}	Total	<i>B</i>	\bar{B}	Total	<i>B</i>	\bar{B}	Total	<i>B</i>	\bar{B}	Total
Positive (<i>A</i>)	18	18	36	31	20	51	47	13	60	96	51	147
Negative(\bar{A})	35	230	265	85	255	340	124	238	362	248	719	967
Total	53	248	301	116	275	391	171	251	422	344	770	1114

VIII. DATA ANALYSIS AND RESULTS

The data analysis was assisted using SAS version 8 software and the results of semi-parametric

roc analysis with their graphs are shown in table 2 below.

Table 2 : Results of Semi-Parametric Roc Analysis of The Data

Trimesters	1 st	2 nd	3 rd	All
Cutoff value of GCT with max AUC	184	177	179	179
Sensitivity with 95% CI	50.00 (44.35-55.65)	60.78 (55.94-65.62)	78.33 (74.4-82.26)	65.31 (62.51-68.1)
Specificity with 95% CI	86.79 (82.97-90.62)	75.00 (70.71-79.29)	65.75 (61.22-70.27)	74.35 (71.79-76.92)
PPV with 95% CI	33.96 (28.61-39.31)	26.72 (22.34-31.11)	27.49 (23.23-31.74)	27.91 (25.27-30.54)
NPV with 95% CI	92.74 (89.81-95.67)	92.73 (90.15-95.3)	94.82 (92.71-96.94)	93.38 (91.92-94.84)
Max. AUC with 95% C.I.	0.684(0.59-0.77)	0.6789(0.61-0.75)	0.7204(0.65-0.77)	0.6983(0.66-0.74)
$n_{\bar{D}}$	265	340	362	967
n_D	36	51	60	147
$\hat{\beta}$	1.578	1.446	1.430	1.409
\hat{u}	1.170	1.007	0.966	0.932
Predicted Probability(π_{it})	0.6857	0.7101	0.8234	0.9210

χ^2 value at one (1) DF and the 95% C.I indicates highly statistically significant relationship(strong degree of association) between screening test results and state of nature or condition (GDM) for all the trimesters.

For all the trimesters, ROC curve analysis showed that (see Fig.1-Fig 4), results were statistically significant at $p < 0.05$ with 95% of C.I.

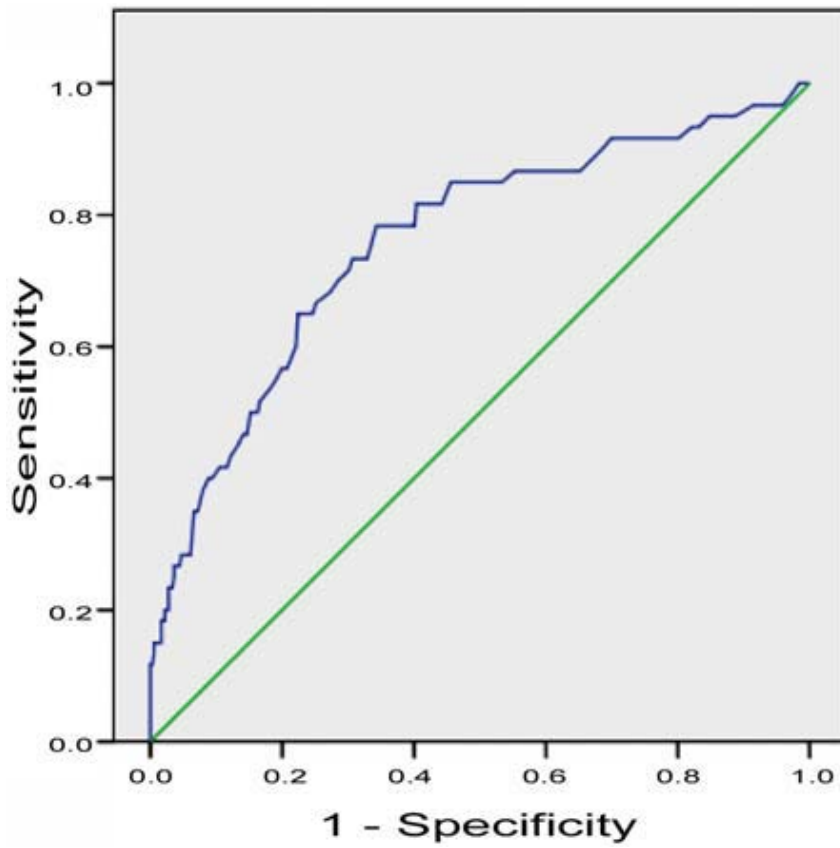


Figure 1 : ROC curve of the 1st trimester,

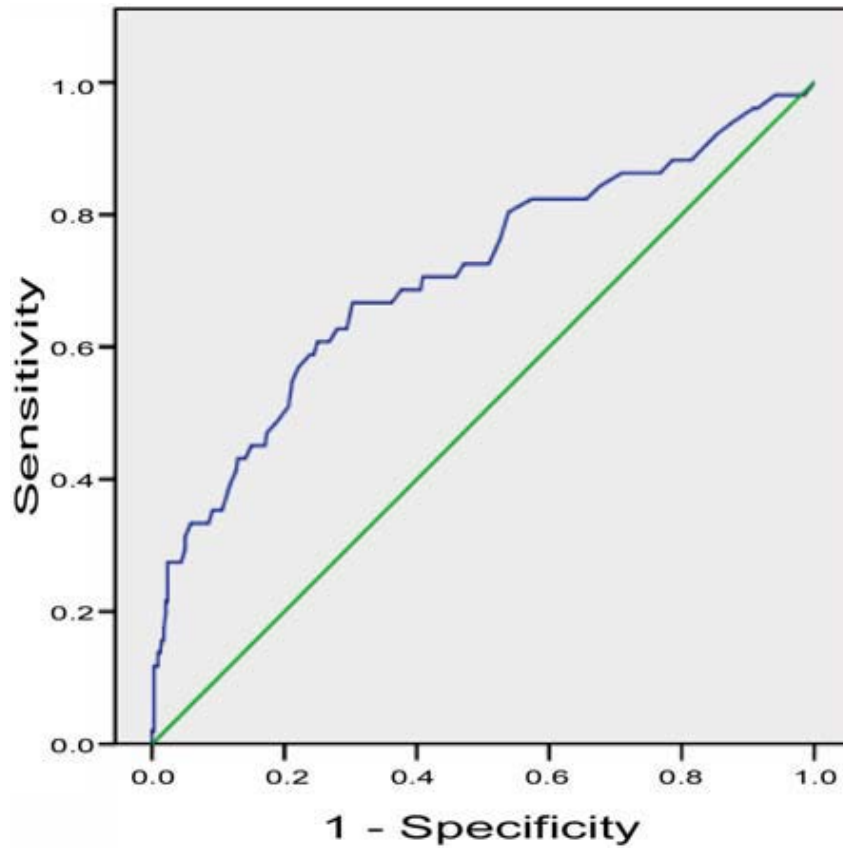


Figure 2 : ROC curve of the 2nd trimester

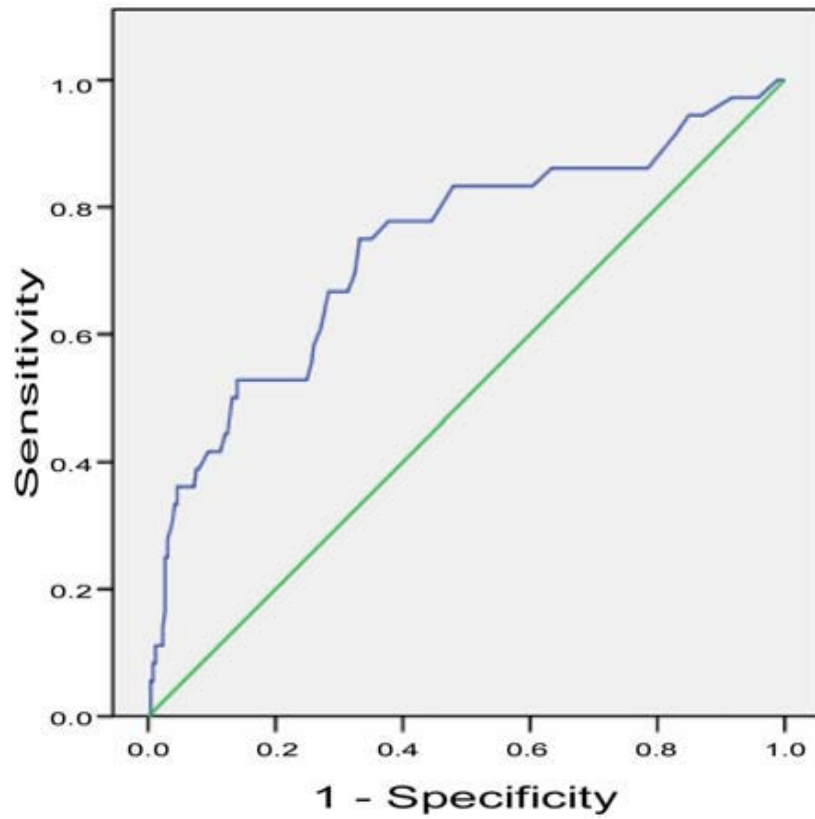


Figure 3 : ROC curve of the 3rd trimester

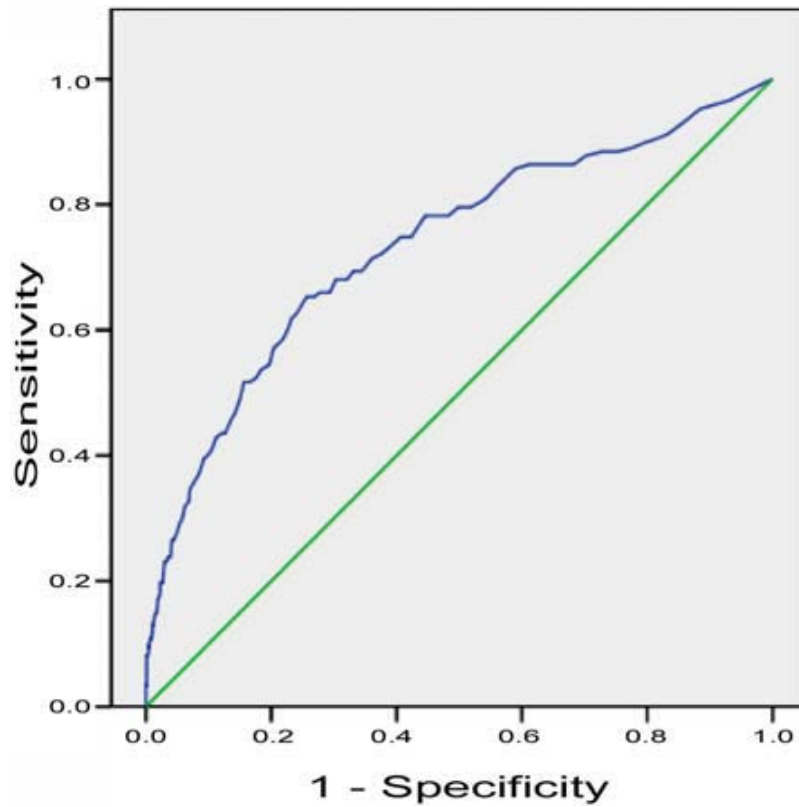


Figure 4 : ROC curve of all trimesters

IX. DISCUSSION

In the present study the cutoff values of GCT in 1st, 2nd, 3rd, and all trimesters were 184, 177, 179, and 179 mg/dl respectively. These values were higher than the previous reports obtained outside Nigeria that recommended the use of 50g GCT level at 130-140 mg/dl for screening of GDM in pregnant women at risk for GDM between 24-28 weeks of gestation (Friedman et al, 2006; Berger et al, 2002; Miyakoshi et al, 2003; Vitoratos et al, 1997). Also Vitoratos et al (1997) and Tanir et al (2005) recommended 126 mg/dl and 185 mg/dl respectively in their study. These are due to differences in race and nutrition of the populations involved. This study also showed that semi-parametric GLMM method provided reliable, unbiased, and consistent estimates for the parameters and AUC. Similar results were obtained by Colak et al (2012).

X. SUMMARY AND CONCLUSIONS

ROC analysis revealed varying cut-off values of 184, 177, 179 and 179 mg/dl for the 1st, 2nd, 3rd and all trimesters and a common cut-off value of 177 mg/dl is chosen for screening 50 grams GCT irrespective of the trimester and is rather suitable for high BMI or obese pregnancy. These variable cutoff values of 50g GCT for screening of GDM is because of increasing weight as pregnancy progresses. Race and nutrition of the population causes differences in cut-off values of 50g GCT for screening women at risk for GDM. High values of NPV such as 92.73-94.82%, indicates the existence of low false negative. Semi-parametric procedure of obtaining predicted probabilities from GLMM because the predicted probabilities of this method have a high statistical efficiency since for all the trimesters, there exist statistical significance. These estimators showed high statistical efficiency. A common cut-off value of 177 mg/dl is recommended for screening 50 grams GCT irrespective of the trimester. Based on the findings in this study, pregnant women from thirty years of age, have greater number of risk of getting GDM at their 2nd and 3rd trimester than those in their 1st trimester of gestation age. It is advised that such category of women should start living healthy life style. Semi-parametric method is preferred to other methods for estimating ROC and constructing AUC because it is more superior in terms of simplicity and accuracy of results. It is therefore recommended.

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GLOBAL JOURNAL OF MEDICAL RESEARCH: K
INTERDISCIPLINARY

Volume 15 Issue 1 Version 1.0 Year 2015

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

Online ISSN: 2249-4618 & Print ISSN: 0975-5888

Prostate Cancer Screening Should Men be Screened for Prostate Cancer?

By Sangeetha Bobba

Introduction- Prostate cancer has the highest incidence of all cancers in Australian men following bowel cancer. Hence prostate cancer screening would be an ideal preventative measure. However, there are both arguments for and against such screening. This report will discuss both arguments and come to a conclusion.

The World Health Organisation (WHO) defines the purpose of screening as to identify the presence of a specific cancer in an individual that does not demonstrate any symptoms. Australia currently employs the WHO's screening program criteria to determine whether a particular illness should be screened.

GJMR-K Classification: NLMC Code: QZ 20.5



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Prostate Cancer Screening

Should Men be Screened for Prostate Cancer?

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I. INTRODUCTION

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The World Health Organisation (WHO) defines the purpose of screening as to identify the presence of a specific cancer in an individual that does not demonstrate any symptoms. Australia currently employs the WHO's screening program criteria to determine whether a particular illness should be screened.

II. WORLD HEALTH ORGANIZATION PRINCIPLES OF SCREENING

World Health Organization guidelines were published in 1968, but are still applicable today.

1. The condition should be an important health problem.
2. There should be a treatment for the condition.
3. Facilities for diagnosis and treatment should be available.
4. There should be a latent stage of the disease.
5. There should be a test or examination for the condition.
6. The test should be acceptable to the population.
7. The natural history of the disease should be adequately understood.
8. There should be an agreed policy on who to treat.
9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10. Case-finding should be a continuous process, not just a "once and for all" project.

Prostate cancer screening satisfies all these criteria. Consequently it would be advantageous in terms of cost-benefit for Australia to employ a universal prostate cancer screening program.

Most screening procedures are non-invasive in order to make them cost-effective and convenient for individuals. Screening modalities including breast exams, mammography, pelvic exams, digital rectal

exams and blood tests require no preparation by the individual needing screening.

As no medical investigations are perfect including screening modalities, there are several adverse effects associated with screening. Consider a case in which an individual's prognosis is the same with or without screening. This individual may experience a longer duration of psychological and physical harm associated with the knowledge of illness and fruitless investigations and treatment. All investigations and screening results have a potential for false negatives and false positives. In the former instance, the individual may become complacent in the identification of symptoms and warning signals while in the latter situation, the individual may be subjected to unnecessary invasive diagnostic tests and procedures. The legal and ethical issues regarding disclosure to insurance companies and potential employers also requires consideration as it may potentially lead to discrimination and psychological harm.

A summary of the potential adverse effects of universal prostate cancer screening (Health Matters, 2013):

- Stress and anxiety caused by false positive screening results
- Unnecessary investigation and treatment of false positive results
- Prolonging knowledge of cancer if no curative treatment can be implemented at that stage in individual cases
- A false sense of security caused by false negatives, which may delay final diagnosis due to individual complacency in recognising symptoms of cancer
- Overuse of scarce medical resources
- Unnecessary and uncomfortable procedures seeking cancer that may be unlikely in individual cases

Prostate Specific Antigen (PSA) used to screen prostate cancer is not 100% specific or sensitive. Randomised Controlled Trials are required to determine the benefit of screening. Of any studies undertaken, both the study design and study analysis must be investigated further before a judgement regarding the effectiveness of screening can be made. Randomised Controlled Trials are considered to produce the most reliable results as they limit bias. The studies must be analysed which ideally should incorporate the

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investigation of possible biases including lead time bias, length bias, selection bias and overdiagnosis bias.

Due to the high incidence and severity of prostate cancer a screening program implementing universal screening would be beneficial in Australia. Such a screening program satisfies the WHO criteria. However, the outcome of a screening program depends on several other factors such as availability, accessibility, health promotion, cost, community attitudes and knowledge. The General Practitioner possesses a crucial role in determining the effectiveness of screening programs. They are important community educators, health promoters and a vital point of contact for individuals considering being involved in screening. In addition, the process of follow-up of positive test results and urgent referral is an imperative role of the General Practitioner in screening programs.

From investigating the significant impact in terms of incidence and prognosis of prostate cancer in Australia it can be deduced that screening would certainly be advantageous. Many studies have demonstrated the benefits of universal prostate cancer screening. The circumscribed screening program satisfies the WHO criteria. However, barriers and adverse effects of screening do exist. These may be overcome by increasing public awareness via health promotion strategies implemented conjointly by Health Professionals and the Australian Government to maximize the potential participation rates and success of a screening program. Currently the Red Book Clinical Guidelines does not recommend screening without symptoms and a discussion with the patient regarding the pros and cons of testing for prostate cancer.

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Volume 15 Issue 1 Version 1.0 Year 2015

Type: Double Blind Peer Reviewed International Research Journal

Publisher: Global Journals Inc. (USA)

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A Review and Emphasis on Emergency Healthcare Systems of Turkey

By Gökem Sarıyer & Mustafa Gökalp Ataman

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Abstract- Emergency health care systems are vitally important. The effective planning of these systems clearly reduces the response time, which is the main factor in saving lives. Thus, it is important to develop this an interactive area of research.

The main goal of this study is to review the state of research on emergency health care systems of Turkey. Furthermore, by highlighting the deficiencies in the Turkish literature in the area, this study aims to stimulate the, interest of researchers.

This study reviews the literature, classifying studies into three areas: evaluation of 112 emergency ambulance services use, determining on optimal ambulance locations, and predictions of call volume.

Although there are some studies related with first two areas subjects, it is important to draw attention to the last of these.

Keywords: ambulance, deployment, emergency medicine, health care, local health, prediction.

GJMR-K Classification: NLMC Code: W 74.1



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A Review and Emphasis on Emergency Healthcare Systems of Turkey

Görkem Sarıyer ^α & Mustafa Gökalg Ataman ^σ

Abstract- Emergency health care systems are vitally important. The effective planning of these systems clearly reduces the response time, which is the main factor in saving lives. Thus, it is important to develop this an interactive area of research.

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Keywords: ambulance, deployment, emergency medicine, health care, local health, prediction.

I. INTRODUCTION

Emergency health-care systems is a chain of different tasks, which start with emergency help and rescue, and are followed by with ambulance transportation, emergency services of hospitals, and rehabilitation services (1). Ambulance transportation plays a key role in this chain. Ambulance transportation of emergency health-care systems exists in all developed and developing countries. In the United States, the emergency call number is 911, while in in European countries and Turkey the number 112 is used (2).

The importance of emergency health-care systems is unquestioned in a society since appropriate and efficient first aid intervention saves lives. Time is the most vital factor which affects the efficiency of first aid intervention; minutes, even seconds can save lives. Therefore, this is an interactive area of research which needs further attention.

In recent years, there has been an increased awareness of emergency health-care systems, especially 112 ambulance systems in Turkey. There are, however, only a limited number of published articles in this area. The main goal of this study is to review this

literature, in an attempt to highlight the need for further research which improves the local health.

In following parts of this study, literature is reviewed based on different sub-topics. The categorization of these sub-topics is as follows: evaluation of 112 emergency ambulance services use, determining on optimal ambulance locations, predictions of call volume.

II. SUBJECT RELATED TOPICS

a) *Evaluation of 112 emergency ambulance services use*

In emergency health-care systems, this sub-topic is widely researched in Turkey. In a retrospective study, calls to the number 112 received at Bursa State Hospital Emergency Service within the period of January 1993-May 1995 are analyzed. The analysis showed that call frequencies increase according to the age of the patient; almost 50% of the cases involve older people. The analysis also summarized the frequent reasons of calling as: 78.3% cerebrovascular disease, 13% cardiovascular disease, and 7.4% traffic accident (3). Another study was designed to determine the clinical characteristics of patients who applied to 112 services with dermatological disorders in Kayseri in 2011. This study showed that in 112 service calls for dermatological disorders were relatively common (4). The use of 112 emergency ambulance services in Konya and Turkey in general between the years 2007 and 2009 was compared in (5). According to this study, approximately 70% of the ambulance calls were carried out for medical purposes, while the following most frequent reason was traffic accidents. Konya was found to have results that are close to or above the country average for each evaluated criteria, such as timely intervention, transfer to hospital, ex-left onside, ex-transfer to morgue, mission aborted, transfer by another vehicle, wrong calls, transfer from hospital to another (5). A study conducted by Yıldız and Durukan has analyzed patients transported to emergency departments of hospitals via ambulances. Due to the continuous need for ambulances to transport patients to emergency departments, this study aimed to determine the appropriateness of transportation via ambulances. For this aim, a prospective study was prepared, which surveyed 524 patients transported to Firat University Faculty of Medicine Emergency Department between 26th May of 2004 and 5th September of 2004. The mean

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arrival time in this study, was 32.17 minutes. Patients were classified as trauma, medical emergencies, or cardiopulmonary arrest. This study concluded that, during ambulance transportation, transportation rules, airway safety, and cervical immobilization were not taken into consideration appropriately (6). Another study was performed to evaluate 112 call services in another province of Turkey, Tekirdağ. The observations of this retrospective study covering the years 2001, 2002, and 2003 suggested that use of 112 services increased by 33% between 2001 and 2002, and 27% between 2002 and 2003. Most frequent reasons for using these services were determined as trauma and cardiovascular orders (7). In their study, Zenginolet. al. examined ambulance orders between the years 2006-2008 in Gaziantep city. According to this study, the maximum number of calls was observed from 6-25 years old for males and above 65 years old for females, call numbers increased every year, and most frequent reasons were classified as medical reasons and traffic accidents (8). In order to evaluate the level of awareness of the emergency call number and utilization of emergency services, Ekşi and Torlakpiloted studies in two Turkish cities, İzmir and Antalya. 616 respondents from İzmir and 291 respondents from Antalya were surveyed using face-to-face interviews. In this study, the level of awareness of the availability of the ambulance emergency service was observed as 89.4%, where it was only 13.5% for the coast guard. Additionally, males, the young and educated were found to use these services more frequently compared to the other sections of the population (9).

Use of 112 services by an older people is specifically analyzed in literature. Among these, the aim of (10) was to evaluate the ambulance use in İzmir between 2004 and 2005. According to this paper, the use of ambulance services by older people is 5 times higher than younger people, and the most frequent reasons are medical conditions and traffic accidents. Furthermore, ambulance use in Turkey, even in İzmir (1.48%), is much lower compared to developed countries, and therefore it is important to develop pre-hospital emergency services. Another study has mentioned that during the first 50 years of 21st century, the world population aged 65 and older is expected to increase three-fold. Thus, caring for old people is one of the most important goals of health-care systems. This descriptive study surveyed patients 65 years and older, who used the 112 services in a province of Turkey, Samsun. This study has shown that cardiovascular, neurologic, and respiratory problems were the most frequent reasons of 112 ambulances use, and highlighted the importance of monitoring and reporting the use of this service (11). In a final descriptive study, patients of 65 years of age and over who used 112 services in Sivas in 2006 were surveyed. This study has shown that the highest level of requests occurred in

January between 10:00 and 12:00 am, and the most common reasons for calls were cardiovascular, neurological, and respiratory problems (12).

b) Determining on optimal ambulance locations

Considerable attention has been paid to the problem of how to best deploy ambulances within a municipality to minimize the response times to emergency calls. In determining the optimal location for ambulances, some optimization models and geographic information systems (GIS) have been proposed in the literature. In their study, Selim and Özkarahan (13) mentioned the need to either increase the number of vehicles or to improve the deployment of existing vehicles in order to decrease the response time of ambulances, which is an important performance measure for emergency service systems. Since increasing the number of vehicles is not always feasible, due to budget constraints, the more efficient deployment of ambulances is more feasible. In their paper, Selim and Özkarahan have proposed a linear deterministic covering-based location model based on two models, the Maximal Backup Coverage Model (14) and the Capacitated Maximal Covering Model (15), respectively created by Hogan and Revelle, and Pirkul and Schilling. Selim and Özkarahan finally tested their model through the sequential solution technique of multiple objective decision making. This model can be used to determine ambulance locations or deployment (13). Another study mentioned that especially for the crowded cities with heavy traffic such as İstanbul, the planning of ambulance location is crucially important. The Backup Double Covering Model, which depends on Set Covering and Maximal Covering location problems, was proposed in the study. It was only possible to obtain the optimal solution for the single period model, whereas for large scale problems with a large number of decision variables and constraints, this model failed to obtain optimal solutions. Thus, a further three heuristic methods have been applied to find the optimal ambulance locations of İstanbul (16).

Geographic Information Systems is also widely used in ambulance deployment. GIS was used in analyses to determine the optimum route for ambulances to reach the incident scene in Isparta. Network topology map of Isparta urban center was constructed to determine optimum routes for ambulances according to various scenarios through ArcGIS 9.0 software. These analyses suggested the creation of new 112 ambulance station points in the required locations (17). In a similar study, a database was developed for traffic accident records of Isparta-Antalya-Burdur national road between 1996-1999, using MS Excel software. Since special coordinates were required, rather than GIS, GPS measurements were made for each traffic accident site. The observations of this study can be summarized as follows: traffic

accidents generally occurred in tangent sections of roads, there was an increase in traffic accidents in day-time and clear weather conditions, and fatal accidents generally occurred on the periphery of the city of Antalya (18). In their study, Erden and Coşkun determined optimal locations of fire stations, and have conducted a multi-criteria site analysis, based on mentioned criteria weights in GIS environment. Sensitivity and robustness analyses were also given in the study. They concluded that, using these models, decision-makers can find optimal locations of fire stations (19).

c) Predictions on Call Volume

This issue is important in planning of Emergency Health Care Systems. In order to plan ambulances effectively, it is important to know not only the optimal locations of the ambulances, but also demand for a specific time interval. To estimate demand for ambulances for a specific time interval, the total number of emergency calls in this interval needs to be estimated. In addition, accurate predictions on call volume allows effective 112 Call Center planning. Combining these benefits, the conclusion is that accurate call volume predictions considerably reduces the response time of ambulances.

Studies have been developed to predict emergency calls or arrival rate. A benchmark study documented an emergency service, using a simple moving average to twenty previous observations: the previous four weeks, from the previous five years (20). Matteson et. al. introduced a more complex method which combines integer-valued time series models with dynamic latent factor structure, to forecast emergency call arrival rates. In order to quantify the impact of reduced forecast errors, they designed a queueing model simulation. This simulation model performed better when the call volume predictions used were more accurate (21). Another study developed time series models of call volume to the emergency medical service in a Canadian city with the objective of offering simple and effective models which can be used in simulating the emergency services (22). Trudeau et. al. classified four main areas of ambulance service operations planning : demand forecasting, scheduling, optimal locations of ambulance points, and simulation as an evaluation tool (23).

Although prediction on call volume of emergency services is an important subject, it has not received any attention in Turkey so far. One of the main goals of this paper is to highlight this deficiency in the literature, in order to stimulate research interest.

III. CONCLUSIONS

Studies on Emergency Health Care Systems of Turkey are reviewed in this article. Since the awareness of people on these systems has just been started to increase, there are only a few of published studies in

this area which are gathered around the two categories of evaluation of 112 emergency ambulance services use, and determining on optimal ambulance locations. However, planning the Emergency Health Care Systems in an effective manner, which sharply decreases the response time of ambulances, considerably depends on demand forecasting or the 112 call volume prediction. Thus, this study aims to draw attention of researchers on this deficiency while reviewing the literature.

a) Conflict of interest

No conflict of interest was declared by the authors.

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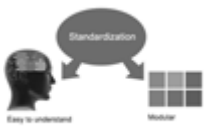
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16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

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21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.



27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium through which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

INFORMAL GUIDELINES OF RESEARCH PAPER WRITING

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.



Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

- Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

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- Align the primary line of each section
- Present your points in sound order
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- Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.



Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript-- must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

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- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.



- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
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Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

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- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently. You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.



Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
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- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

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- In spite of position, each table must be titled, numbered one after the other and complete with heading
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- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.



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<i>Methods and Procedures</i>	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
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<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



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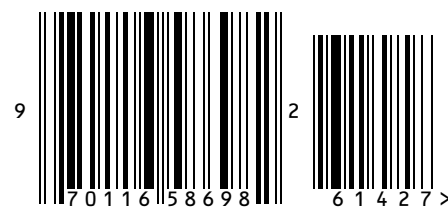
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