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ABOUT THE JOURNAL

Aims and Scope

Asian Archives of Pathology (AAP) is an open access, peer-reviewed journal. The journal was first published in 2002 under the Thai name "วารสารราชวิทยาลัยพยาธิแพทย์แห่งประเทศไทย" and English name "Journal of the Royal College of Pathologists of Thailand". The journal is a publication for workers in all disciplines of pathology and forensic medicine. In the first 3 years (volumes), the journal was published every 4 months. Until 2005, the journal has changed its name to be "Asian Archives of Pathology: The Official Journal of the Royal College of Pathologists of Thailand", published quarterly to expand the collaboration among people in the fields of pathology and forensic medicine in the Asia-Pacific regions and the Western countries.

The full articles of the journal are appeared in either Thai or English. However, the abstracts of all Thai articles are published in both Thai and English languages. The journal features letters to the editor, original articles, review articles, case reports, case illustrations, and technical notes. Diagnostic and research areas covered consist of (1) **Anatomical Pathology** (including cellular pathology, cytopathology, haematopathology, histopathology, immunopathology, and surgical pathology); (2) **Clinical Pathology (Laboratory Medicine)** [including blood banking and transfusion medicine, clinical chemistry (chemical pathology or clinical biochemistry), clinical immunology, clinical microbiology, clinical toxicology, cytogenetics, parasitology, and point-of-care testing]; (3) **Forensic Medicine (Legal Medicine or Medical Jurisprudence)** (including forensic science and forensic pathology); (4) **Molecular Medicine** (including molecular genetics, molecular oncology, and molecular pathology); (5) **Pathobiology**; and (6) **Pathophysiology**.

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On the other hand, if any authors request a printed copy of the journal issue containing the articles, each of the copied journals costs 450 bahts for Thai authors and 30 United States dollars (USD) for international authors.

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MANUSCRIPT REVIEWERS

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ORIGINAL ARTICLE

Forensic age-at-death estimation using the sternal junction in Thai adults: An autopsy study

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Abstract

One of the main parameters in the analysis of skeletal remains in forensic anthropological cases is the estimation of age. This study aimed to investigate the correlation between age and the fusion status of the sternal junction. This cross-sectional study was carried out on 184 sterna from 94 females and 90 males obtained from known-age cadavers in the Thai population. By direct observation, the fusion stage of the manubrio-sternal and sterno-xiphoidal junctions was studied and divided into unfused and fused joints. The results showed that a large proportion of the sterna remain unfused throughout adulthood, with fusion observed in both young and old cadavers. Significant differences in the rate of fusion between the sexes were observed. None of the sterna under 30 years of age in females and 32 years of age in males showed fusion of the manubrio-sternal and sterno-xiphoidal junctions. Based on the variability of the sternal fusions observed in this study, we highlighted a very limited role of the sternum alone in the estimation of age in the Thai population.

Keywords: Age estimation, Sternum, Fusion of bones, Forensic anthropology

Introduction

Age is one of the biological profiles that is particularly useful in narrowing the number of missing persons compared to the profile of the deceased [1]. In adults, age estimation focuses not only on bone degeneration but also the appearance and fusion of the ossification

centers of the bones [2]. Several regions of the body have been studied to make the most accurate age estimation, such as pubic symphysis, auricular surface, cranial suture, sternal end of the rib, and medial end of the clavicle [3-8]. The sternum, however, may be a reliable source of information and can offer useful information for age estimation in some cases with this bone.

The sternum has been considered a potential application in forensic age estimation in young adult and adult skeletons. Most of the authors studied direct observation of the fusion of manubrio-sternal and sterno-xiphoidal junctions in different population groups [9-21]. All of these studies found that the manubrio-sternal and sterno-xiphoidal junctions fused at different times. Studies in this regard have been carried out in the Chinese[10], Indian population[11-15], South African[16], Turkish[17-18], Egyptian[19], Spanish[20], Japanese[21] and mixed population (mainly British)[9]. For the Thai population, Monum et al. [22] developed a model for age estimation in the Thai male population using radiological analysis of chest plate ossification. However, the question arises of whether the results obtained from the radiological examination can be compared with those from direct observation. To the best of our knowledge, there was no study of age estimation using direct observation of the sternum in a Thai population. The results from the non-Thai population may be unreliable with the Thai population due to variations in genetics and environment.

Therefore, the aim of this study was to examine the sterna of a Thai population for the fusion of manubrio-sternal and sterno-xiphoidal junctions using the direct observation method, and to determine the applicability of this method for age-at-death estimation.

Materials and Methods

This study has been approved by the Research Ethics Committee of the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand (Protocol No.950/2564 (IRB2) on December 1st, 2021). Informed consent was obtained from the legal heirs before collecting the sterna. Between December 5th, 2021 and November 10th, 2022, the intact sterna were removed from the deceased who underwent autopsy in the Forensic Pathology Unit, Department of Forensic Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University. All of the deceased were Thai nationals, 20 years of age or older. Because it is generally recognized that the sternal body segments develop fully and unite at the age of 20-25, the age of 20 was chosen [23-24]. The age and nationality were approved by identification documents issued by the Thai government. The deceased with pathological sterna or injuries at any location in the examined area was excluded from this study.

After manual maceration of the surrounding muscles and soft tissues, the sterna were allowed to macerate in warm water for 4 weeks. All residual soft tissue was removed from the bones using a gentle brush and running water to prevent any damage to the bone surface. The bones were allowed to dry at room temperature. The sterna were studied with a naked

eye examination and the fusion status of their junctions was observed. The manubrio-sternal and sterno-xiphoidal junctions were classified as unfused or fused (Figure 1). Fusion was considered when it was discovered that a part of the joint space was fused. It was deemed nonfusion if none of the surfaces was found to be fused. The observers did not know the age and sex of the sample during their examination. Additionally, a blind test was carried out with a sample of known age.

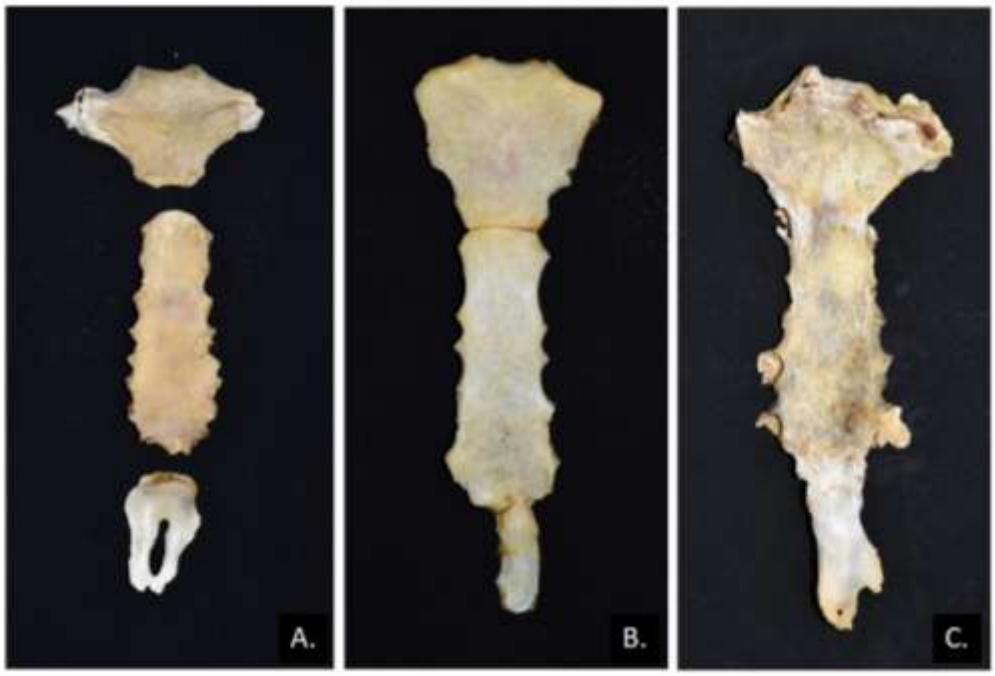

Figure 1: Photograph showing nonfusion (A.) and fusion (B. and C.) of sternal elements

All statistical analyses were performed with SPSS statistical software, version 20.0 (SPSS, Inc., Chicago, IL, USA). A p-value of less than 0.05 was considered statistically significant. Descriptive statistics was used to illustrate the occurrence of fusion throughout the sample and Chi-squared tests were used to find variations between the sexes and the fusion rates. To clarify the correlations between the fusion rates and the true age, point-biserial correlation coefficient was carried out. The association between age above and below 45 and the state of fusion of the manubrio-sternal and sterno-xiphoidal junctions was also evaluated using an odd ratio. The age of 45 was chosen as the halfway point between data entries in the sample of this study and the midpoint between the various reports of fusion in the literature [(16)].

Results

A total of 184 sterna were included, consisting of 94 females (20 to 83 years) and 90 males (20 to 84 years). The mean age of females and males in this study population was 44.62 (SD = 17.20) years and 49.07 (SD = 16.59) years, respectively.

Tables 1 and 2 demonstrate the fusion of the manubrio-sternal and sterno-xiphoidal junctions in various age groups among females and males. Direct observation of the manubrio-sternal junction revealed that 46.74% (n = 86) of the sterna had a fusion of the joint. The earliest fusion of manubrio-sternal junction was reported at 30 years of age in females and 36 years in males, while nonfusion was observed until the age of 83 years in females and 84 years in males. In female, the manubrio-sternal junction fused at a mean age of 54.94 years (SD = 13.91), while males showed a mean age of fusion of 55.33 years (SD = 13.02).

Table 1 shows the fusion of the female sterna in the various age groups

Age (years)	Number	Manubrio-sternal junction		Sterno-xiphoidal junction	
		Nonfusion (%)	Fusion (%)	Nonfusion (%)	Fusion (%)
20-29	13	13 (100%)	0 (0%)	13 (100%)	0 (0%)
30-39	15	8 (53.3%)	7 (46.7%)	11 (73.3%)	4 (26.7%)
40-49	21	9 (42.9%)	12 (57.1%)	15 (71.4%)	6 (28.6%)
50-59	19	5 (26.3%)	14 (73.7%)	10 (52.6%)	9 (47.4%)
60-69	14	2 (14.3%)	12 (85.7%)	6 (42.9%)	8 (57.1%)
>70	12	5 (41.7%)	7 (58.3%)	6 (50%)	6 (50%)
Total	94	42 (44.7%)	52 (55.3%)	61 (64.9%)	33 (35.1%)

Table 2 shows the fusion of the male sterna in the various age groups

Age (years)	Number	Manubrio-sternal junction		Sterno-xiphoidal junction	
		Nonfusion (%)	Fusion (%)	Nonfusion (%)	Fusion (%)
20-29	23	23 (100%)	0 (0%)	23 (100%)	0 (0%)
30-39	20	13 (65%)	7 (35%)	12 (60%)	8 (40%)
40-49	13	7 (53.8%)	6 (46.2%)	7 (53.8%)	6 (46.2%)
50-59	13	4 (30.8%)	9 (69.2%)	8 (61.5%)	5 (38.5%)
60-69	14	7 (50%)	7 (50%)	5 (35.7%)	9 (64.3%)
>70	7	2 (28.6%)	5 (71.4%)	1 (14.3%)	6 (85.7%)
Total	90	56 (62.2%)	34 (37.8%)	56 (62.2%)	34 (37.8%)

A total of 67 (36.4%) sterna demonstrated a fused sterno-xiphoidal junction, consisting of 33 (35.1%) female sterna and 34 (37.8%) male sterna. The oldest sterna with unfused sterno-xiphoidal junction were 76 years old in females and 78 years old in males, whereas the youngest sterna with complete fusion were 30 years old in females and 32 years old in males. In female, the sterno-xiphoidal junction fused at a mean age of 57.09 years (SD = 12.92), while males showed a mean age of fusion of 55.59 years (SD = 15.47). It was noted that, with advancing age, more males and females had sterna with fused manubrio-sternal and sterno-

xiphoidal junction. Number of sterna with fusion of the manubrio-sternal and sterno-xiphoidal junctions in each age group are illustrated in Figure 2.

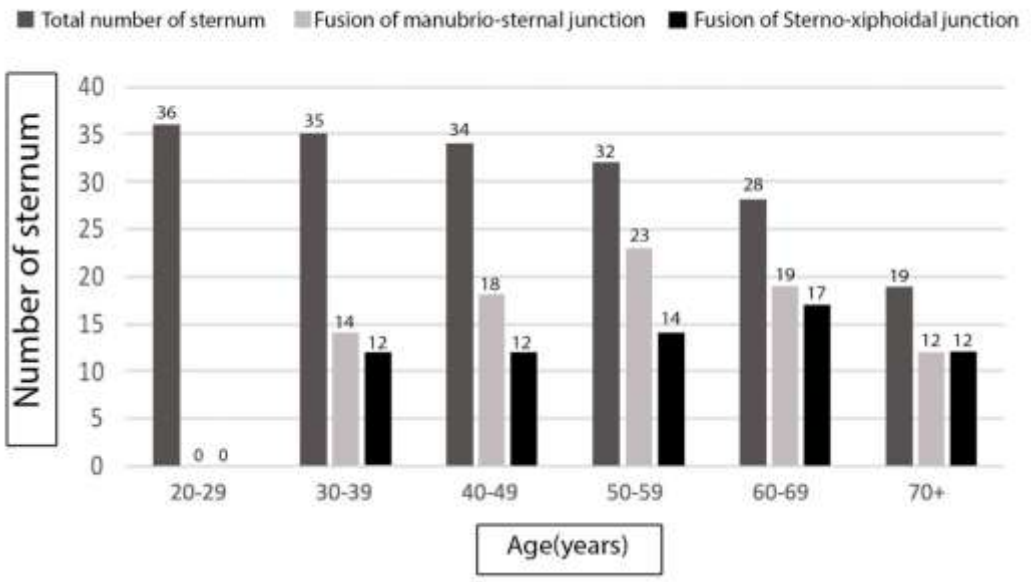

Figure 2: Age distribution of the study population and the proportion of sterna with the fusion of manubrio-sternal and sterno-xiphoidal junctions

Statistical significance was observed in the rate of fusion between sexes, both at the manubrio-sternal and sterno-xiphoidal junctions ($p<0.001$). A moderate correlation was observed for the correlation between age and fusion stages of sternal elements ($R_{pb} = 0.547$, $p<0.001$). An odd ratio was calculated to assess the association between either above and below the age of 45 years and the fusion state of the manubrio-sternal and sterno-xiphoidal junctions. Statistically significant differences were observed between the age of fusion above and below 45 years for the manubrio-sternal and sterno-xiphoidal junctions ($p < 0.001$). Females and males with age over 45 years were 4.14 and 4.44 times more likely to have the fusion of manubrio-sternal junction than those with age below 45 years, respectively. In addition, females and males over the age of 45 had fusions of the sterno-xiphoidal junctions at rates of 5 and 4.14 times higher than those under 45 years of age.

Discussion

Age estimation is one of the four essential components needed to aid in personal identification, and therefore, a number of skeletal regions are analyzed to enhance the age estimation methods and accuracy rates. This study sought to determine whether there was a correlation between age and the fusion of manubrio-sternal and sterno-xiphoidal junctions in a Thai population. The present study showed that the fusion of the manubrio-sternal and sterno-xiphoidal junctions increased with advancing age. Significant variations were observed from person to person and the fusion of the manubrio-sternal and sterno-xiphoidal junctions might not occur at all. Throughout adulthood, most sterna remain unfused, and fusion is seen in both young and old people. Therefore, the fusion rate of both the manubrio-sternal and sterno-xiphoidal junctions was not a reliable age indicator. Previous studies have reported similar results on the high variability in the fusion rate of the manubrio-sternal and sterno-xiphoidal junctions [11-22]. Table 3 summarizes the studies about the fusion of manubrio-sternal and sterno-xiphoidal junctions. The studies focusing on age estimation from the sternum have yielded contradictory results. The possible reason for such differences may be the genetic difference of the population included in the study. Furthermore, it is crucial to note that there is confusion regarding the definition of fusion in the literature. The assessment of fusion may be affected by the differences between the methodological approach used (radiological or direct observations).

Table 3: Summary of studies of the fusion of the manubrio-sternal and sterno-xiphoidal junctions

Study	Nationality	Assessment	Sample size	manubrio-sternal fusion ages	sterno-xiphoidal fusion ages

Chandrakanth et al. (11)	South Indian	Gross	118	Starts at 31 (F), 35 (M) Unfused even up to 75 (F), 70 (M)	Starts at 30 (F, M) Unfused even up to 46 (F), 48 (M)
Singh and Pathak (12)	North-west Indian	Gross	343	Starts at 17 (F), 19 (M) Almost fused at 38 (F), 42 (M)	Almost fused at 46 (F), 50 (M)
Chopra et al. (13)	North Indian	Gross	200	Starts at 35 (F), 29 (M)	Starts at 26 (F, M)
Manoharan et al. (14)	South Indian	Gross	100	Highly variable	Starts at 40 (F), 32 (M) All fused at 60 (F, M)
Sahu et al. (15)	Eastern Indian	Gross	102	Starts at 17 (F), 19 (M) Unfused up to 80 (F), 78 (M), Highly variable	Starts at 25 (F), 23(M) Unfused up to 85
Bacci et al. (16)	South African	Gross	461	Highly variable	Highly variable
Oktay and Aytaç (17)	Turkish	CT	200	Highly variable	-
Study	**Nationality**	**Assessment**	**Sample size**	**manubrio-sternal fusion ages**	**sterno-xiphoidal fusion ages**
Bolatlı et al. (18)	Turkish	CT	700	Starts at 10-19 (F, M)	Starts at 10-19 (F, M)
Ali et al. (19)	Egyptian	CT	165	Starts at 25-35 (F, M) Unfused up to 55-65 (F, M)	Starts at 25-35 (F, M) Unfused up to 55-65 (F, M)
Macaluso and Lucena (20)	Spanish	Radiograph	122	Starts at 23 (F), 29 (M) Unfused up to 91 (F), 88(M)	Starts at 22 (F), 29 (M) Unfused even up to 91 (F), 67 (M)
Monum et al. (21)	Japanese	CT	320	Highly variable	Highly variable
Monum et al. (22)	Thai (male only)	Radiograph	136	15-81	15-70

The present study	Thai	Gross	184	Starts at 30 (F), 36 (M) Unfused even up to 83 (F), 84 (M)	Starts at 30 (F), 32 (M) Unfused even up to 76 (F), 78 (M)

In this study, a significant difference between sexes was observed in the fusion rate of the manubrio-sternal and sterno-xiphoidal junctions. Fusion of the manubrio-sternal junction occurred proportionately more frequently in females (55.3%) than in males (37.8%). A greater proportion of sterna in different age groups of females revealed a fusion of the manubrio-sternal junction than the sterno-xiphoidal junctions. These findings were inconsistent with previous studies by Singh and Pathak [12] and Bacci et al. [16], who found a higher number of fused sterna in males than in females. This could be a result of unrecognized alterations in bone metabolic turnover and related biochemical changes in the joint [16]. In addition, males showed an earlier and, much higher number of fused sterno-xiphoidal junctions in all age ranges compared to females. This may be due to differences in breathing patterns between sexes, with males showing a more active movement of the abdomen and possibly more mechanical stress on the xiphoid process because several breathing muscles attach to this structure [26-27]. This finding also indicates that the age estimation from the fusion rate of sterno-xiphoidal junctions is less reliable in males than in females.

In this study, the fusion of the manubrio-sternal junction occurs in all age groups after the age of 30 years in females and 36 years in males. Fusion at the manubrio-sternal junction can occur through primary or matrical fusion (not age-related) and secondary or sclerotic fusion (probably age-related) [9,11,16-17]. The primary cartilaginous joint between the manubrium and mesosternum can be obliterated during early life and this process is thought to be the cause of the matrical fusion. On the other hand, sclerotic fusion is assumed to be the outcome of pathological processes because it occurs in late adulthood and involves the obliteration of a secondary cartilaginous joint between the manubrium and mesosternum [9]. Thus, the matrical fusion is taken into account as a potential cause of the high variance in the fusion time of the manubrio-sternal junction. Previous literature recommended using radiographic investigation for the analysis of manubrio-sternal junction because this technique is more effective to distinguish between matrical and sclerotic fusion [11,16,25]. Direct observation of the fusion of the manubrio-sternal junction should be interpreted cautiously and should not be directly compared to the results of the radiographic examination. In this study, the fusion status of the sternum was evaluated using the direct observation approach, which is most often used in forensic anthropological examination in developing countries because it is more cost-effective and suits field work. Due to funding limitations and inadequate facilities, a radiographic examination could not be performed on the sternum in the present study. This may be considered a limitation of this study. Examinations of the unfused state should be

considered more reliable than those of the fusion state when using direct observation to estimate the age of the sternum.

Most earlier investigations discovered that the age at which different sternal elements fused was variable, making age estimation based on sternal elements unreliable. However, the fusion of the manubrio-sternal and sterno-xiphoidal junctions in this study may have some potential to differentiate between young people and older adults. This study attempted to express a proportion of the likelihood of age between fusion and nonfusion of the manubrio-sternal and sterno-xiphoidal junctions. The results showed that females or males with fused sternal elements are approximately 4 times more likely to be older than those without fused sternal elements. Furthermore, the fusion of the sterno-xiphoidal junctions starts as early as 30 years in females and 32 years in males, whereas the earliest fusion of the manubrio-sternal junction was reported at 30 years in females and 36 years in males. This is useful for estimating the age of the Thai population. For example, if an unknown sternum is discovered in a forensic anthropological setting, it can be assumed that an unidentified female or male was no older than 30 years if she or he has no sternal fusion at all. All techniques have validity, but the best strategy for estimating age is one that recognizes and considers all available evidence [28-29]. We believe that these values, rather than serving as age range indicators, may be employed in forensic anthropological analysis to support conventionally recognized age estimation techniques.

There is a need for additional studies using large sternum samples or using a combination of direct and radiological examinations among the Thai population. Studies on Thai sub-adult sterna are also required as non-metric traits offer more precise and reliable results for sex and age determination than adult traits.

In conclusion, this study found that the age at which the manubrio-sternal and sterno-xiphoidal junctions fused was highly variable, resulting in a low effectiveness of using this method as a forensic age-at-death estimation in the Thai population. Based on the results of this study, we recommend using the nonfusion of sternal joints to indicate ages lower than 30 years of age in females and 32 years of age in males.

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ORIGINAL ARTICLE

Prevalent study and hematological parameters of new born with G-6-PD deficiency in 2021 at Nopparat Rajathanee Hospital

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Abstract

Glucose-6-phosphate dehydrogenase deficiency (G-6-PD deficiency) is inherited as an X-linked recessive pattern. G-6-PD deficiency causes premature destruction of red blood cells during exposure to oxidative stress produced from Fava bean or certain drugs. A late treatment in severe cases of G-6-PD deficiency might lead to acute hemolytic anemia and then develop as renal failure. To avoid a possible harmful reaction, it is necessary to screen for G-6-PD deficiency in patients who will be treated with certain drugs and who are doubted about icterus This study was aimed to investigate the prevalence of G-6-PD deficiency and hematological parameters in G-6-PD deficiency patients in Nopparat Rajathanee Hospital, Bangkok, Thailand. The G-6-PD Deficiency was screened by fluorescent spot test in 1-year-old patients by retrospective collecting data from 1 January 2021 to 31 December 2021 and were selected from 514 children (295 males, 219 females). Results showed the G-6-PD deficiency patients were 0.97% (5 of 514) and the normal G-6-PD were 99.03% (509 of 514).

The prevalence of G-6-PD deficiency were 0.010, with 0.014 in male (4 male-G-6-PD deficiency patients) and 0.005 in female (1 female-G6PD deficiency patients) and the prevalence rate of G-6-PD deficiency were 0.97%, 1.4% of male and 0.5% of female. The hematological parameters in G-6-PD deficiency patients were mean ±SD of RBC (x106/uL) 4.94±0.58, Hb (g/dL) 17.5±2.37, HCT (%) 48.84±5.88, and MCV (fL) 99.04±7.10, and were

compared to the mean hematologic results in the normal reference values of under 1 year of age at Nopparat Rajathanee Hospital. The mean of hematologic results of newborn pediatric with G-6-PD deficiency found that RBC, Hb and HCT were in the normal reference range except MCV.

In summary the information obtained from this study would be beneficial to individually treated patients especially those with G-6-PD deficiency and lead to a proper treatment by suitable drugs well as having the G-6-PD deficiency epidemiology data of the community in Nopparat Rajathanee Hospital, Bangkok, Thailand.

Keywords: G-6-PD deficiency, Prevalence, Hematological parameters

การศึกษาความชุกและค่าทางโลหิตวิทยาของเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD ในโรงพยาบาลนพรัตนราชธานี ปี 2564

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ส่งต้นฉบับ: *วันที่ 12 เดือนกรกฎาคม พ.ศ. 2565*
รับลงตีพิมพ์: *วันที่ 9 เดือนกุมภาพันธ์ พ.ศ. 2567*
ตีพิมพ์เผยแพร่: *วันที่ 1 เดือนมิถุนายน พ.ศ. 2567*

บทคัดย่อ

ภาวะพร่องเอนไซม์ G-6-PD เกิดจากการถ่ายทอดทางพันธุกรรมที่ผิดพลาดของโครโมโซม X เป็นสาเหตุที่ทำให้มีการแตกของเม็ดเลือดแดงในร่างกายเมื่อได้รับอนุมูลอิสระจากภายนอก เช่น ถั่วปากอ้า หรือยาบางชนิด เป็นต้น ซึ่งก่อให้เกิดภาวะโลหิตจางและอาจส่งผลให้เกิดภาวะไตล้มเหลวตามมา ดังนั้น เพื่อหลีกเลี่ยงอันตรายที่อาจเกิดขึ้นในผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD ที่กำลังได้รับการรักษาด้วยยาบางชนิดจึงมีความจำเป็นที่จะต้องตรวจคัดกรองภาวะพร่องเอนไซม์ G-6-PD รวมทั้งทารกแรกคลอดและเด็กที่สงสัยสาเหตุภาวะตัวเหลือง วัตถุประสงค์ของการศึกษาครั้งนี้คือ การศึกษาความชุกของภาวะพร่องเอนไซม์ G-6-PD และค่าทางโลหิตวิทยาในผู้ป่วยภาวะพร่องเอนไซม์ G-6-PD ในโรงพยาบาลนพรัตนราชธานี โดยการเก็บข้อมูลย้อนหลัง 1 ปี (พ.ศ. 2564) คัดเลือกจากเด็กแรกเกิดถึงอายุไม่เกิน 1 ปี จำนวน 514 ราย (เพศชาย 295 ราย เพศหญิง 219 ราย) ซึ่งส่งตรวจภาวะพร่องเอนไซม์ G-6-PD ด้วยวิธี Fluorescent spot testing พบว่าให้ผลปกติ (normal, non-G-6-PD deficiency) 509 ราย (เพศชาย 291 ราย, เพศหญิง 218 ราย) ผลพร่องเอนไซม์ G-6-PD (G-6-PD deficiency) 5 ราย คิดเป็นร้อยละ 99.03 และ 0.97 ตามลำดับ พบความชุกของภาวะพร่องเอนไซม์ G-6-PD ทั้งหมดคิดเป็น 0.010 โดยในเพศชายพบความชุกคิดเป็น 0.014 (4 ราย) เพศหญิงพบความชุกคิดเป็น 0.005 (1 ราย) และ อัตราความชุกทั้งหมดคิดเป็น 0.97, 1.4 และ0.5 ตามลำดับ นอกจากนี้ค่าทางโลหิตวิทยาในผู้มีภาวะพร่องเอนไซม์ G-6-PD ได้แก่ ค่าเฉลี่ย±ส่วนเบี่ยงเบนมาตรฐาน ของเม็ดเลือดแดง (x106/uL), ฮีโมโกลบิน (g/dL), ปริมาณอัดแน่นของเม็ดเลือดแดง (%), ปริมาตรของเม็ดเลือดแดงโดย เฉลี่ย (fL) มีค่า 4.94±0.58, 17.5±2.37, 48.84±5.88 และ 99.04±7.10 ตามลำดับ เมื่อเปรียบเทียบค่าเฉลี่ยผลทางโลหิตวิทยากับค่าอ้างอิงปกติของเด็กทั้งเพศชายและเพศหญิง อายุต่ำกว่า 1 ปี ที่โรงพยาบาลนพรัตนราชธานีใช้ พบว่าค่าเฉลี่ยทางโลหิตวิทยาเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD มีค่า RBC, HB, HCT อยู่ในช่วงค่าอ้างอิงปกติ ส่วน MCV สูงกว่าช่วงค่าอ้างอิงปกติ

โดยสรุป ข้อมูลที่ได้จากการศึกษานี้เป็นข้อมูลที่เป็นประโยชน์ สำหรับการพยากรณ์และการรักษาผู้ป่วย โดยเฉพาะผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD จะได้รับการหลีกเลี่ยงการรักษาภาวะ และ/หรือโรคอื่นๆ โดยการเลือกใช้ชนิดของยาที่เหมาะสม ขณะเดียวกันทำให้ได้ข้อมูลทางระบาดวิทยาของภาวะพร่องเอนไซม์ G-6-PD ของโรงพยาบาลนพรัตนราชธานีอีกด้วย

คำสำคัญ: ภาวะพร่องเอนไซม์ G-6-PD ความชุก ค่าทางโลหิตวิทยา

บทนำ

ภาวะโลหิตจางจากการพร่องเอนไซม์ G-6-PD (Glucose-6-phosphate dehydrogenase deficiency) เป็นภาวะโลหิตจางจากการขาดเอนไซม์ในเม็ดเลือดแดงที่พบได้บ่อยที่สุด[1] มีการถ่ายทอดพันธุกรรมผ่านทาง X โครโมโซม ความผิดปกติเกิดจากการกลายพันธุ์ของยีน G-6-PD ซึ่งสามารถพบได้ทั่วโลกและมีอุบัติการณ์สูง

ในคนไทย ในแต่ละภาคของประเทศไทยจะมีอุบัติการณ์ของการพร่องเอนไซม์ G-6-PD แตกต่างกันไปในช่วงร้อยละ 3-17[2] G-6-PD เป็นเอนไซม์ตัวแรกใน Hexose monophosphate pathway (HMP) ทำหน้าที่ในการเปลี่ยนGlucose-6-phosphate (G-6-PD) และ NADP ให้เป็น 6-phosphogluconate (6-PG) และ NADPH ซึ่ง NADPH มีบทบาทในการรักษาสภาวะของ glutathione ให้อยู่ในรูป reduced form และ reduced glutathione นี้เองที่ช่วยทำให้ oxidizing agent (ไฮโดรเจนเปอร์ออกไซด์, Hydrogen peroxide) เปลี่ยนเป็นสารที่ไม่ทำอันตรายต่อเซลล์[3] คนส่วนใหญ่ที่มีภาวะพร่องเอนไซม์ G-6-PD และไม่มีภาวะโลหิตจางจะมีลักษณะรูปร่างของเม็ดเลือดแดงปกติ[4] และไม่มีอาการทางคลินิก แต่อาจจะพบภาวะโลหิตจางได้เป็นครั้งคราวเมื่ออยู่ในภาวะ oxidative stress เช่น ในกรณี infection, inflammation, กรณีได้รับยาหรือสารเคมีที่มีคุณสมบัติเป็น oxidizing agent ทำให้ผู้ป่วยไม่สามารถกำจัด oxidizing agent ได้อย่างมีประสิทธิภาพและทำให้เม็ดเลือดแดงเสียสภาพและอาจเกิดการแตกทำลายอย่างเฉียบพลันแบบ acute acquired hemolytic anemia[4-5] กลไกที่ทำให้เม็ดเลือดแดงแตกนั้นเกิดจากการที่ oxidizing agent ที่เซลล์กำจัดไม่หมดไป oxidize ไขมันและโปรตีนที่อยู่บนผิวเซลล์ (cell membrane) เม็ดเลือดแดง รวมทั้งฮีโมโกลบินที่เป็นโปรตีนที่มีมากที่สุดในเม็ดเลือดแดง ทำให้ฮีโมโกลบินแตกออกเป็น heme และ globin และ globin ถูก oxidize เสียสภาพ และจับตัวกันที่ผิวเซลล์ของเม็ดเลือดแดง (Heinz body) ส่งผลให้เซลล์เม็ดเลือดแดงเสียคุณสมบัติตามธรรมชาติ elasticity, deformability ไป และแตก ฉีกขาดได้ง่าย นอกจากนี้เมื่อเซลล์เหล่านี้ผ่านไปที่ม้ามมันจะถูกเซลล์ macrophage ที่อยู่ในม้ามกำจัดส่วนที่ผิดปกติของผิวเซลล์ไป[6] ดังนั้นในผู้ทีมีภาวะพร่องเอนไซม์ G-6-PD เมื่อได้รับยา สารเคมี หรือเกิดภาวะใดก็ตามที่กระตุ้นให้มีการสร้างสารอนุมูลอิสระต่างๆ ขึ้นมาและไม่สามารถกำจัดออกได้ สารดังกล่าวจึงเป็นพิษต่อเซลล์ในร่างกาย โดยเฉพาะอย่างยิ่งเซลล์เม็ดเลือดแดง ก็ทำให้เกิดการแตกเม็ดเลือดแดง (hemolysis) ได้ ซึ่งผู้ป่วยส่วนใหญ่จะไม่มีอาการผิดปกติ ส่วนในรายที่มีอาการผู้ป่วยส่วนใหญ่มักจะมาด้วยภาวะตัวเหลืองในทารกแรกเกิด (neonatal jaundice) และภาวะเม็ดเลือดแดงแตกสลายเฉียบพลัน (acute hemolytic anemia) หลังจากที่ได้รับยา สารเคมี หรือเกิดภาวะใดก็ตามที่กระตุ้นให้มีการแตกสลายของเม็ดเลือดแดง เช่น ภาวะติดเชื้อ ทำให้ผู้ป่วยมีอาการซีดลงฉับพลัน ตัวเหลือง (ทำให้ระดับสารสีเหลืองบิลิรูบินในเลือดสูง) บางรายอาจมีปัสสาวะสีน้ำตาลดำหรือสีโค้ก อาการต่างๆมักเกิดขึ้นภายใน 24-72 ชม. ในรายที่รุนแรงอาจพบว่าปริมาณปัสสาวะออกน้อยลงจนก่อให้เกิดภาวะไตวายฉับพลัน[7] การวินิจฉัยภาวะพร่องเอนไซม์ G-6-PD แพทย์จะทำการพิจารณาซักประวัติคนในครอบครัวที่ป่วยเป็นภาวะนี้หรือภาวะโลหิตจางที่ยังหาสาเหตุไม่ได้และอาจตรวจฮีโมโกลบินในเลือดและปัสสาวะ ตรวจความสมบูรณ์ของเม็ดเลือด เช่น การตรวจเซลล์เม็ดเลือดแดง เซลล์เม็ดเลือดขาว ฮีโมโกลบิน และฮีมาโทคริต ตรวจนับปริมาณเซลล์เม็ดเลือดแดงตัวอ่อน (reticulocyte count) เพื่อดูอัตราการสร้างเซลล์เม็ดเลือดแดงจากไขกระดูก ตรวจวัดระดับบิลิรูบินเพื่อดูระดับอัตราการสลายตัวเซลล์เม็ดเลือดแดงในเลือด ตรวจวัดระดับเอ็นไซม์ G-6-PD

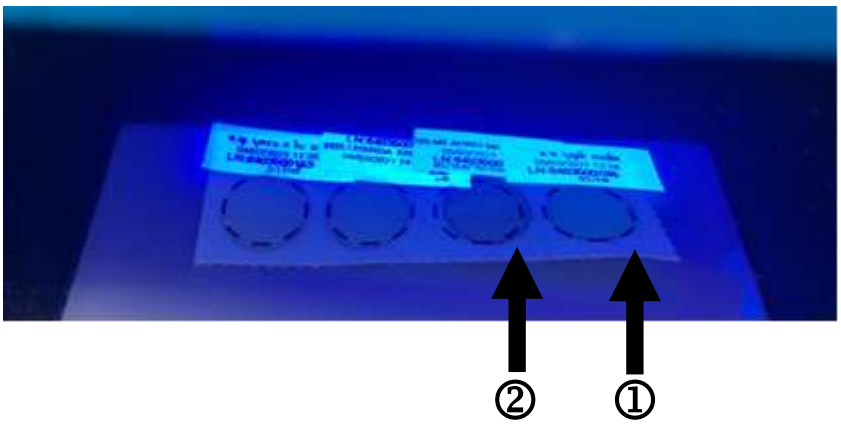
ด้วยเหตุนี้ ในการศึกษาครั้งนี้จึงสนใจศึกษาหาความชุกและค่าทางโลหิตวิทยาในผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD ของเด็กแรกเกิดที่โรงพยาบาลนพรัตนราชธานี ในปี พ.ศ. 2564

วิธีดำเนินการวิจัย

เป็นการศึกษาข้อมูลย้อนหลังเชิงพรรณนา ซึ่งทำการศึกษาในเด็กแรกเกิดทั้งเพศชายและเพศหญิงซึ่งคลอดที่โรงพยาบาลนพรัตนราชธานี เพื่อศึกษาหาความชุกของเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD โดยเก็บข้อมูลจากผลการตรวจวิเคราะห์ในเด็กแรกเกิดที่ได้รับการตรวจภาวะพร่องเอนไซม์ G-6-PD และข้อมูลการรายงานผลค่าพารามิเตอร์ทางโลหิตวิทยาในการตรวจ CBC ด้วยค่าดัชนีเม็ดเลือดแดง (RBC count, Hb, HCT, MCV) ระหว่างวันที่ 1 เดือน มกราคม ถึงวันที่ 31 เดือน ธันวาคม 2564 โดยระบบสารสนเทศทาง

ห้องปฏิบัติการ (LIS) และของโรงพยาบาลนพรัตนราชธานี (HIS) ซึ่งใช้ตัวอย่างเลือดจาก EDTA blood นำไปตรวจวิเคราะห์ด้วยเครื่องมือตรวจวิเคราะห์เม็ดเลือดชนิดอัตโนมัติ (Sysmex XN 3000) (รูปที่ 1) บันทึกค่าดัชนีเม็ดเลือดแดงต่างๆ ลงในแบบบันทึกผลการตรวจวิเคราะห์ โดยการตรวจ CBC นั้นจะทำในทันทีเมื่อได้รับเลือดขณะเลือดสดใหม่ (fresh) เพื่อให้ได้ค่าที่ถูกต้องมากที่สุด และทดสอบภาวะพร่องเอนไซม์ G-6-PD ด้วยวิธี fluorescent spot test (R&D Diagnostics) (รูปที่ 2)

รูปที่ 1 เครื่องตรวจวิเคราะห์เม็ดเลือดชนิดอัตโนมัติ (Sysmex XN 3000)
ที่มา : https://www.sysmex-europe.com/products/products-detail/xn-3000.html



รูปที่ 2 แสดงการเรืองแสงในภาวะพร่องเอ็นไซม์ G-6-PD และภาวะปกติ ด้วยวิธี fluorescent spot test ภาวะปกติพบการเรืองแสง (หมายเลข 1) ส่วนภาวะพร่องเอนไซม์ G-6-PD จะไม่เรืองแสง (ตามหมายเลข 2)

การวิเคราะห์ทางสถิติ

นำข้อมูลทั้งหมดมาวิเคราะห์หาค่าทางสถิติ ดังนี้ ค่าเฉลี่ย (mean) ค่ามัธยฐาน (median) ส่วนเบี่ยงเบนมาตรฐาน (standard deviation) โดยทำการศึกษาจากประชากรทั้งหมดที่มาคลอดที่โรงพยาบาล

ตามเกณฑ์คัดเลือก เพศ ร้อยละของจำนวนให้ผลการทดสอบเป็นผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD และแยกเพศ ร้อยละของอัตราความชุกของทั้งหมดและแยกเพศ สัดส่วนระหว่างเพศชายต่อเพศหญิงในกลุ่ม G-6-PD deficiency ศึกษาค่าเฉลี่ยทางโลหิตวิทยาในผู้ที่มีภาวะพร่องเอนไซม์ เปรียบเทียบกับช่วงค่าอ้างอิงปกติ

ผลการวิจัย

ข้อมูลผลการตรวจภาวะพร่องเอนไซม์ G-6-PD ในเด็กแรกเกิดที่โรงพยาบาลนพรัตนราชธานีของผู้ป่วยย้อนหลัง ตั้งแต่วันที่ 1 มกราคม 2564 ถึงวันที่ 31 ธันวาคม 2564 จากระบบสารสนเทศทางห้องปฏิบัติการ (LIS) สามารถแบ่งตัวอย่างเป็นสองกลุ่ม กลุ่มที่ 1 คือ G-6-PD deficiency จำนวน 5 ราย เป็นเพศชาย 4 ราย เป็นเพศหญิง 1 ราย กลุ่มที่ 2 คือ normal G-6-PD จำนวน 509 ราย เป็นเพศชาย 291 ราย เป็นเพศหญิง 218 ราย ดังรายงาน (ตารางที่ 1)

ตารางที่ 1 แสดงจำนวนเด็กแรกเกิดในโรงพยาบาลนพรัตนราชธานี ในปี พ.ศ. 2564 ที่ทำการตรวจภาวะพร่องเอนไซม์ G-6-PD

	Normal (ราย)	G-6-PD deficiency (ราย)	Total (ราย)
Male	291	4	295
Female	218	1	219
Total	509	5	514

ตารางที่ 2 แสดงข้อมูลแสดงค่าทางโลหิตวิทยาของเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD

		RBC ($x10^6$uL)	Hb (g/dL)	HCT (%)	MCV (fL)
Total	N	4	4	4	4
	Mean	4.94	17.5	48.84	99.04
	Median	5.06	17.9	49.1	97
	SD	0.58	2.37	5.88	7.10

(N: number of sample, M: Male, F: Female, RBC: Red Blood cell Count, Hb: Hemoglobin, HCT: Hematocrit, MCV: Mean Corpuscular Volume)

จากตารางที่ 2 เป็นการแสดงผลการศึกษาค่าทางโลหิตวิทยาในเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD พบว่า มีค่าเฉลี่ยของ RBC 4.94±0.58 (x106/µL), Hb 17.5±2.37(g/dL), HCT 48.84±5.88 (%) และ MCV 99.04±7.10 (fL)

ตารางที่ 3 แสดงจำนวนเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD ในปี พ.ศ. 2564

Result	**N**	**ร้อยละ**		**N_{all} = 514**	
Deficiency	5	0.97%	M	4	0.78%
			F	1	0.19%

(D: G-6-PD Deficiency, N_{all}: Number of all population in 2021, M: Male and F: Female)

จากตารางที่ 3 แสดงจำนวนเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD จำนวนทั้งหมด 5 ราย เป็นเพศชาย 4 ราย และเพศหญิง 1 ราย คิดเป็นร้อยละ 0.97, 0.78 และ 0.19 ตามลำดับ

ตารางที่ 4 แสดงความชุกของการเกิดภาวะพร่องเอนไซม์ G-6-PD ในปี พ.ศ. 2564

Result			**N_{all}= 514,**	**M_{all} = 295,**	**F_{all} = 219**
				Prevalence	Prevalence Rate
D	**M**	4	0.78%(4/514*100)	0.014(4/295)	1.4 (4/295*100)
	F	1	0.19%(1/514*100)	0.005(1/219)	0.5 (1/219*100)
	Total	5	0.97%(5/514*100)	0.010(5/514)	0.97 (5/514*100)

(D: G-6-PD Deficiency, M: Male, F: Female, N_{all}: Number of all population in 2021, M_{all}: Number of male population in 2021, F_{all}: Number of female population in 2021)

จากตารางที่ 4 แสดงค่าความชุกของเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD พบว่ามีความชุกในเด็กแรกเกิดทั้งหมด เด็กเพศชาย และเด็กเพศหญิง เท่ากับ 0.01, 0.014 และ 0.005 ตามลำดับ และคิดเป็นอัตราความชุกในเด็กแรกเกิด 100 ราย คือ 0.97, 1.4 และ 0.5 ตามลำดับ

อภิปรายผลการวิจัย

ข้อมูลในการวิจัยครั้งนี้ทำให้พบว่าเขตพื้นที่โดยรอบของโรงพยาบาลนพรัตนราชธานีมีอัตราความชุกและข้อมูลทางระบาดวิทยาของเด็กแรกเกิดเพื่อใช้ในการพยากรณ์และการรักษาผู้ป่วยโดยเฉพาะเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD จะได้หลีกเลี่ยงการรักษาภาวะหรือโรคอื่นๆ โดยการเลือกใช้ชนิดของยาที่เหมาะสม และลดอาการตัวเหลืองในเด็กทารก สามารถนำข้อมูลที่ได้ ไปใช้ให้คำปรึกษา ป้องกันและควบคุมโรคต่อไป โดยวิธีที่ใช้ตรวจนี้มีความถูกต้อง แม่นยำ สูง ทำได้ง่าย สะดวก รวดเร็ว มีความไวและความจำเพาะสูง และการตรวจยืนยัน (confirmatory testing) เพิ่มเติมสามารถหาพาหะโรคภาวะพร่องเอนไซม์ G-6-PD ในผู้หญิงที่มีการทำงานของเอนไซม์ G-6-PD ปกติหรือเกือบปกติ ซึ่งพาหะสามารถส่งต่อไปยังรุ่นต่อๆ ไปได้ และสามารถตรวจหาความรุนแรงได้ด้วย

สรุปผลการวิจัย

การทดสอบภาวะพร่องเอนไซม์ด้วยวิธี fluorescent sport test ตั้งแต่ 1 มกราคาคม 2564 ถึง 31 ธันวาคม พ.ศ. 2564 จากประชากรทั้งหมด 514 ราย เป็นเพศชาย 295 ราย และเพศหญิง 219 ราย ให้ผลการทดสอบเป็นผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD จำนวนทั้งหมด 5 ราย เป็นเพศชาย 4 ราย และเพศหญิง 1 ราย คิดเป็นร้อยละ 0.97, 0.78 และ 0.19 ตามลำดับ พบว่ามีความชุก 0.01, 0.014 และ 0.005 ตามลำดับ คิด

เป็นอัตราความชุกในเด็กแรกเกิด 100 ราย คือ 0.97, 1.4 และ 0.5 ตามลำดับนอกจากนั้นเมื่อคิดสัดส่วนระหว่างเพศชายต่อเพศหญิง ในกลุ่ม G-6-PD deficiency พบว่ามีอัตราส่วน 4:1 โดยพบอัตราความชุกมีแนวโน้มไปในทิศทางเดียวกันกับที่มีการรายงานผู้มีภาวะพร่องเอนไซม์ G-6-PD จากโรงพยาบาลศูนย์ตรัง จำนวนทั้งหมด 102 ราย เป็นเพศหญิง 12 รายและเพศชาย 90 ราย คิดเป็นร้อยละ 3.33, 0.39 และ 2.94 ตามลำดับ[8]

ผลการศึกษาค่าทางโลหิตวิทยาในผู้ที่มีภาวะพร่องเอนไซม์ G-6-PD พบว่า RBC (x106/µL), Hb (g/dL), HCT(%) และ MCV (fL) เท่ากับ 4.94±0.58, 17.5±2.37, 48.84±5.88 และ 99.04±7.10 ตามลำดับ เมื่อเทียบกับค่าอ้างอิงปกติ ดังนี้ RBC 4.20-5.4 (x106/µL), Hb 14-20 (g/dL), HCT 43-63 (%) และ MCV 80-95 (fL) พบว่าค่าเฉลี่ยผลทางโลหิตวิทยาเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD มีค่า RBC, Hb, HCT อยู่ในช่วงค่าอ้างอิงปกติ ส่วน MCV สูงกว่าช่วงค่าอ้างอิงปกติเล็กน้อย

กิตติกรรมประกาศ

การศึกษาวิจัยเรื่องการศึกษาความชุกและค่าทางโลหิตวิทยาในเด็กแรกเกิดที่มีภาวะพร่องเอนไซม์ G-6-PD ในโรงพยาบาลนพรัตนราชธานี ระหว่างเดือนมกราคม 2564 ถึง เดือนธันวาคม 2564 ที่สำเร็จลุล่วงไปได้ตามวัตถุประสงค์ในครั้งนี้ ด้วยความช่วยเหลือและสนับสนุนจากบุคคลหลายท่าน ผู้วิจัยใคร่ขอกล่าวขอบพระคุณมา ณ ที่นี้

ขอขอบพระคุณบุพการี ที่ช่วยให้กำลังใจตลอดการศึกษาวิจัยนี้

ขอบพระคุณ พันเอกหญิง ผู้ช่วยศาสตราจารย์ ภัสรา อาณัติ หัวหน้าภาควิชาชีวเคมี กองการศึกษา วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า ที่ให้คำแนะนำ คำปรึกษา ข้อแก้ไขด้านต่างๆ ในการเขียนผลงาน

ขอบพระคุณนางสาวดวงใจ ตันติยาภรณ์ หัวหน้ากลุ่มงานพยาธิวิทยาคลินิกและเทคนิคการแพทย์ ที่ให้คำแนะนำและให้คำปรึกษาด้านต่างๆ ตลอดจนชี้แนะแนวทางในการแก้ปัญหาให้ลุล่วงตลอดการศึกษาวิจัย

ขอบพระคุณนายจรัลพัฒน์ ธรรมนนท์กุล นักวิชากาคอมพิวเตอร์ที่ให้ความอนุเคราะห์ในการเก็บข้อมูลจากโรงพยาบาลจนสำเร็จด้วยดีตลอดการศึกษา

ขอบคุณเจ้าหน้าที่ทุกคนในหน่วยงานโลหิตวิทยา กลุ่มงานพยาธิวิทยาคลินิกและเทคนิคการแพทย์ ที่ช่วยเหลือและให้กำลังใจตลอดการศึกษาวิจัยนี้

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ORIGINAL ARTICLE

A PROSPECTIVE STUDY OF CONCORDANCE AND DISCORDANCE BETWEEN CLINICAL AND AUTOPSY DIAGNOSES BY POSTMORTEM EXAMINATION IN A TERTIARY CENTRE IN SOUTH WEST NIGERIA

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Abstract

The autopsy is the veritable means of ascertaining the actual primary diagnosis that succinctly explains the sequence of events leading to complications and death in a deceased person. It is referred to as the gold standard and ultimate diagnosis clincher and revealer of secrets. This prospective study of ninety-two (92) deceased persons. Sixty (60/65.2%) were males and 32 (34.8%) were females. Autopsy revealed pathology in the heart in 15 patients (16.1%), multiple organ dysfunction in 11 patients (11.8%), liver in 4 patients (4.3%) and others (cervix) in 2 patients (2.2%). The final anatomical diagnosis of the diseases showed systemic hypertension in 42 patients (45.6%), neoplasms in 19 patients (20.7%), gastrointestinal/liver diseases in 19 patients (20.7%), infections in 9 patients (9.8%), and post-partum haemorrhage in 3 patients (3.3%). There was clinical and autopsy diagnoses concordance in 53 patients (57%) and discordance in 39 patients (41.9%). The concordant rate was highest in cases with complication of systemic hypertension (24 cases; 44.4%), next to it were cases due to infections (15 cases; 27.8%), followed by neoplasms (10 cases; 18.5%) and others including ruptured varices and perforated gastric ulcers (4 cases; 7.4%), commoner in males than females and more frequent within the middle age group (40-59) The discordant cases were mostly cardiopulmonary complication (17 cases; 31.5%) and next to it was infection (11 cases; 20.4%), followed by neoplasms (7 cases; 13.0%) and others (4 cases; 7.4%) most commonly gastrointestinal bleeding. The ability of the autopsy to unravel the correct diagnosis helps to resolve diagnostic dilemmas, foreclose controversies and enable records for crucial decisions for medical treatment.

Keywords: Clinical versus postmortem diagnoses, concordance, discordance, prospective study

Introduction

Clinical diagnosis remains an interminable basis and technical ground for errors and the ensuing unpleasant consequences of embarrassing litigations at all levels of health care delivery

[1–4]. Clinicians attend to quite a number of patients and their state of health are often difficult to diagnose due to potentially difficult clinical presentation [5-6]. Clinicians may have insufficient experience with both common and rare diseases and with varying access to diagnostic investigations. Exact and timely diagnosis anchors upon many factors including the knowledge, experience and skills of the clinicians and the resources available.

A diagnostic error emerges when diagnosis is missed, or is utterly wrong. Diagnoses occur over time rather than at one point in time, including initial assessment, performing and interpreting diagnostic tests, follow up and tracking of diagnostic information as well as medical patient's response, attitudes and engagement, essentially correlating the entire clinical picture to make thoroughly informed decisions.

Clinical diagnoses have been known to be at variance with postmortem diagnoses across the world even with the best technology and expertise [7]. Many factors may be responsible for the dichotomy between antemortem and postmortem diagnoses. These include the expertise, all round experience and case exposure of the attending physician [5]. Others include the available investigative technology, atypical presentations and the unique constitution of individual patients [6]. Missed diagnoses and misdiagnoses continue to evoke questions that may generate medicolegal challenges cum untoward outcomes such as professional discipline, panels of enquiry and outright embarrassing litigations for clinical negligence and medical malpractice with payment of crippling compensations for damages[8]. It may also evoke the application of the doctrine of vicarious liability against the employer who may be implicated by association with the errant and derelict employee [9]. The best means to ascertain the correctness or otherwise of clinical diagnoses, understand the pathogenesis, pathophysiology of the disease process, correlate morphology with the stage at death, understand the modifying circumstances, the complications, define the exact cause of death and the progression of events leading to death is by the conducting the postmortem examination. The postmortem examination is the gold standard investigation that reveals the true state of events antemortem and sets records straight [10]. It offers a diversity of morphological findings such as affirming the correctness of clinical diagnoses or revealing confounding features such as incidental findings unrelated to the cause of death, evidence of misdiagnoses, missed diagnoses or other findings that could emphasize the indispensability of proper medical history is necessary to correlate autopsy findings with clinical judgment or suggest that the immediate cause of death was unrelated to previously known pathologies in the patient or quite worrisome as cause of death may be at variance with known clinico-pathological condition of the patient[11]. The postmortem examination has been known to emphasize the importance of proper medical history in the correlation of autopsy findings with clinical deductions. Autopsy findings usually influence future clinical managements and the data obtained are relevant in appropriate epidemiological studies, ascertaining the true burden of disease, especially in asymptomatic clinico-pathological disorders, conduct of research to ascertain changing patterns and association of diseases and correlative budgeting in order to enhance proper health care delivery [12].

This study was prospective in nature and entailed the systematic documentation of the findings in a questionnaire form to answer specific questions so as to draw conclusions that could influence better clinical decisions, inform more evidence-based management protocol and modalities that would prevent medical litigations.

Autopsy is germane in revealing all hidden secrets about patient's managements and it is regarded as the gold standard [5,13-14]. It is valued as the most important tools for retrospective quality assessment of clinical diagnosis, the methods by which the diagnoses were formulated, the competence of the managing physician and team as well as a key to education tool [15].

Aims and Objectives

1. To determine the postmortem diagnoses and compare them with antemortem clinical diagnoses in order to ascertain the correlation and correctness of antemortem clinical diagnoses.
2. To determine the presence or otherwise of missed diagnoses
3. To determine the presence of significant diagnoses at postmortem that contributed to the progression of the disease process.

Materials and Methods

A prospective study of the full post mortem dissections done including histological examination were comprehensively reviewed. The antemortem clinical diagnoses were correlated with postmortem diagnoses. The inclusion criteria were all clinical cases of adult patients that died in the hospital with clinical diagnosis and with signed consent for the autopsy while all medico-legal cases, autopsies restricted to single organ or body cavities (limited autopsy) and cases referred from peripheral hospitals with insufficient clinical information and incomplete data were excluded from the study.

Results

A total of four hundred and seventeen (417) requests were received during the study period, out of which one hundred and seventeen (117) were clinical cases. However, only ninety-two (92) fulfilled the inclusion criteria of the study. The remaining 25 cases comprised of 17 paediatric clinical autopsy cases (neonate – 14, under five – 3), 4 limited clinical autopsy and four clinical cases with suspected COVID-19 infection (see table 1). Out of these 92 clinical cases, 21 cases were referred from other facilities and private hospitals to OAUTHC for expert management before their demise while 71 cases were primarily managed at the study centre till their demise.

Out of the 92 clinical cases that underwent autopsy, 60 (65.2%) were males and 32 (34.8%) were female. The patients' mean age was 52.8 years with standard deviation of 14.7 years. The median age was 55.0 years (range, 20 to 79), 17 (18.5%) were young adults, 42 (45.7%) were middle-aged patients while 33 (35.8%) were elderly (See table 2).

The clinical diagnoses of the primary diseases offered by the clinicians revealed that 33 patients (35.9%) had systemic hypertension, 18 patients (19.6%) had infections, 15 patients (16.3%) had neoplasms, 12 patients (13.0%) had gastrointestinal/liver disease and 9 patients (9.7%) had urogenital disease. Musculoskeletal diseases were found in 3 patients (3.3%) and 2 patients (2.2%) accounted for other diagnoses (such as severe haemolytic crises precipitated by malaria and severe anaemia in a hypertensive patient).

A full autopsy was done on all the patients and tissue sections taken from each organ for histopathological examination. The main organ findings of pathology discovered at autopsy which reflected the immediate cause of death showed that lung ranked highest in 22 patients (23.7%) followed by brain in 21 patients (22.6%) and next to it was gastrointestinal tract in 17 patients (18.3%). Furthermore, autopsy revealed pathology in the heart in 15 patients (16.1%), multiple organ dysfunction in 11 patients (11.8%), liver in 4 patients (4.3%) and others (cervix) in 2 patients (2.2%). Final anatomical diagnosis of the diseases also showed systemic hypertension in 42 patients (45.6%), neoplasms in 19 patients (20.7%), gastrointestinal/liver diseases in 19 patients (20.7%), infections in 9 patients (9.8%), and post-partum haemorrhage in 3 patients (3.3%) (See figure 1). Macroscopic/gross finding alone provide the cause of death in 50 patients (54.3%) which was later confirmed by histological examination while histological examination also provided/contributed to the diagnosis of cause of death in 42 patients (45.7%) where gross findings were not definitive.

In 53 patients (57.0%), the autopsy findings confirmed (concordant) the clinical diagnoses suggested by the attending clinicians. In 39 patients (41.9%), the clinical diagnoses stated by the clinicians were discordant with the autopsy findings (See figure 2). The concordant rate was highest in cases with complication of systemic hypertension (24 cases; 44.4%), next to it were cases due to infections (15 cases; 27.8%), followed by neoplasms (10 cases; 18.5%) and others including ruptured varices and perforated gastric ulcers (4 cases; 7.4%). The concordant cases were also noted to be commoner in male than female and more frequent within the middle age group (40-59) (See figure 2 and 3). The discordant cases were mostly cardiopulmonary complication (17 cases; 31.5%) and next to it was infection (11 cases; 20.4%), followed by neoplasm (7 cases; 13.0%) and others (4 cases; 7.4%) most commonly gastrointestinal bleeding.

Table1. Shows the distribution of autopsy types during the study period

Variables	Frequency	Percentage (%)
Medicolegal Autopsy	300	71.8
Clinical Autopsy		
Adult	92	22.0
Paediatrics	3	0.7
Neonatal	14	3.6
Limited autopsy	4	1.0
COVID-19	4	1.0
Total	**417**	**100**

Table 2. Shows socio-demographic distribution

Variable	Frequency	Percentage
Age groups		
20-39yrs	17	18.5
40-59yrs	42	45.7
60-79yrs	33	35.8
Mean age ± SD	54.84± 14.74	100
Gender		
Males	60	65.2
Females	32	34.8

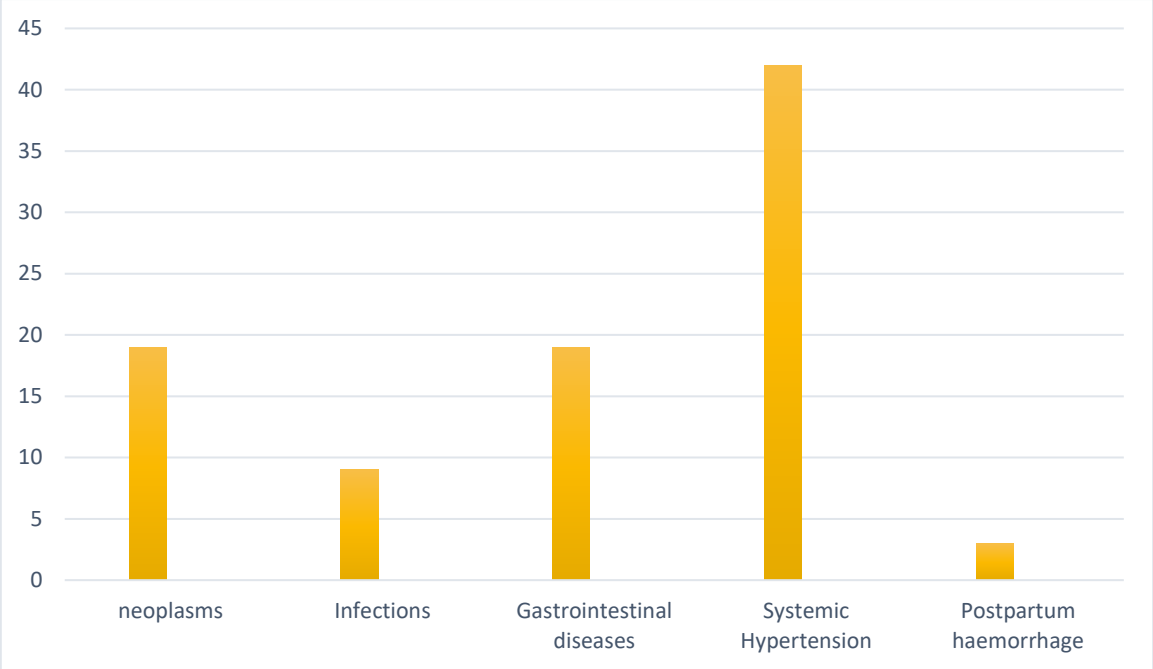

Figure 1. Shows the highlights of the autopsy findings discovered at autopsy.

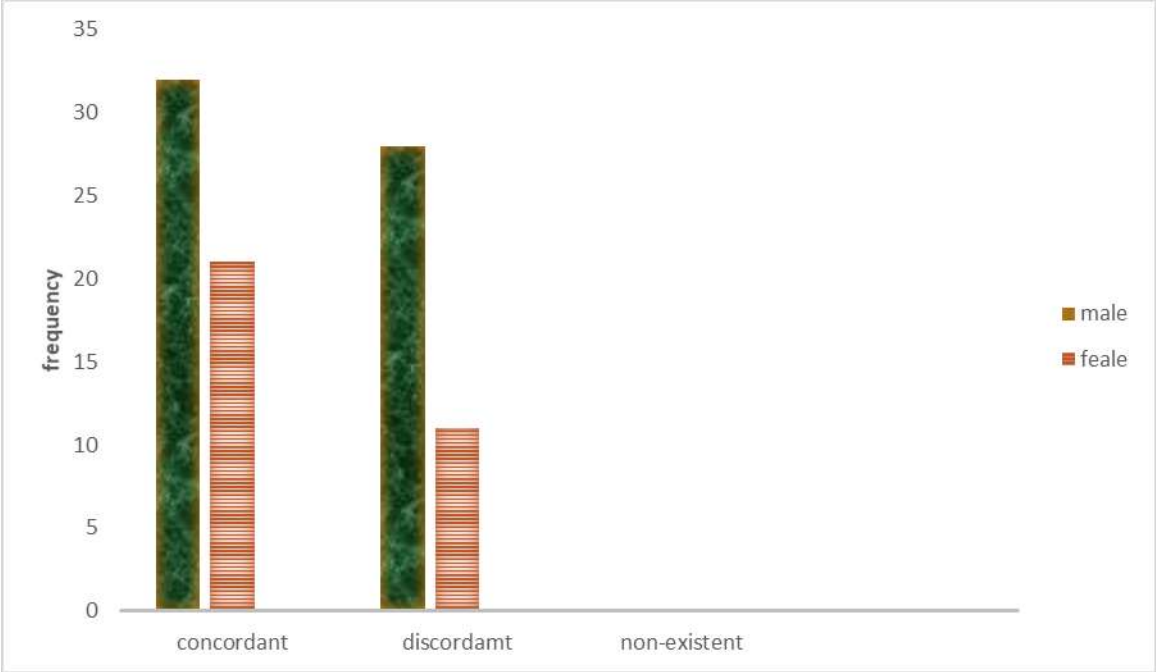

Figure 2. Shows the distribution of concordant and discordant cases in relation to gender.

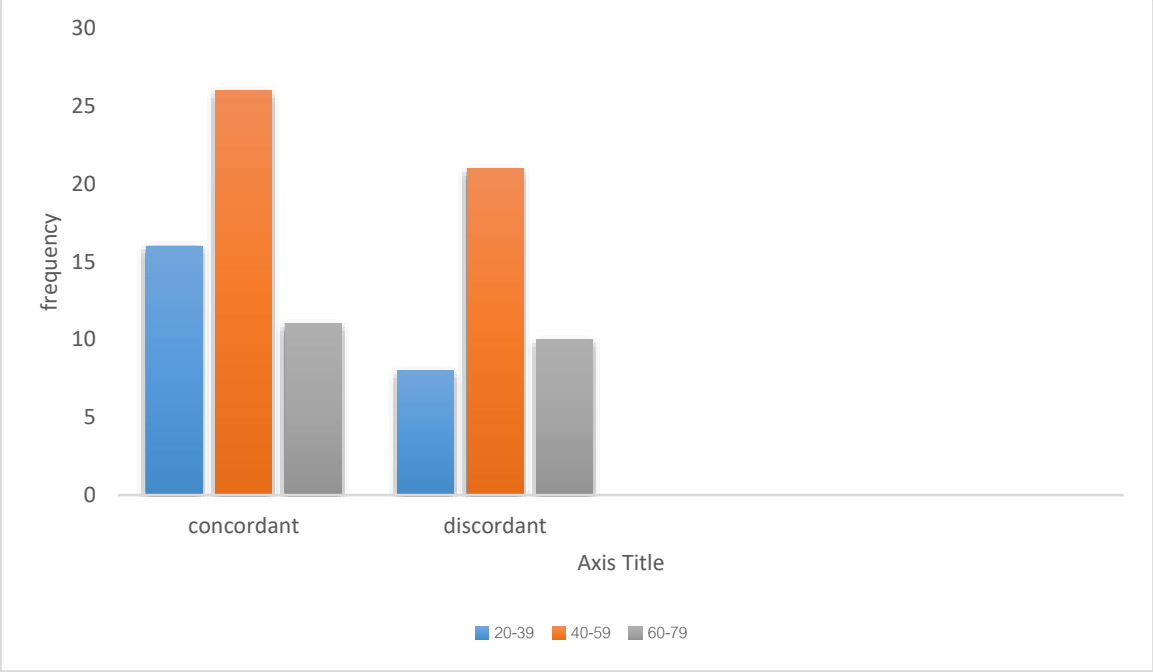

Figure 3. Shows the distribution of the discordant and concordant cases among the age groups.

Discussion

The imperativeness of the right diagnoses in determining the most appropriate mode of management cannot be overemphasized considering the implications in terms of premature deaths, complications and litigations for medical malpractice and clinical negligence [5-7].

Our study showed major and minor discrepancies in two-fifth and about a third, that is 33% to 40% of all the cases respectively. This is quite high when viewed against other studies which showed that major discrepancy rates range from 7% to 50% [16-18]. However, this rate is lower than that found by Silas et al in north-central Nigeria while it is greater than that reported by Kuijpers et al, [10] in Holland, Shojania et al, [19] and Marshall et al [20] in United States in their separate studies. Travor et al[21] recorded a higher major discrepant rate in post-operative deaths to be as high as 50% in their study which is higher than this study although, Baker in United States found major diagnostic errors in 39.7% of autopsies contributing to patient's death in his study[22]. Even studies comparing clinical diagnosis and autopsy diagnosis in intensive care unit patients showed major discrepancy rate ranging from 19.8% to 30%, though lower than this study which may be attributed to a better diagnostic facility (23-24). However, Combes et al recorded a higher rate of major discrepancy of 40% in their study which is fairly close to this study [25]. Also in a systemic review by David et al, he reported 23.5% of clinical missed major diagnosis reflecting the principal cause of death [26]. It suffices to say despite the ranges of missed major diagnoses, discrepancies still exist and does not preclude any clinician and their perceived experience. A similar study by Ojo et al found

a concordance rate of 82.1% between clinical and autopsy diagnoses[27], The concordance rate between clinical diagnosis and autopsy diagnosis was found to be 72.2% in their study[28] while Komolafe et al showed that 25 (40.32%) of their cases were discrepant while 37 (59.68%) cases were concordant[7]. Loughrey et al found that 10% of cases showed major discrepancies at postmortem examination [29]. While Jashnani etal found a discrepancy rate of 9% in their study in India, Ermenc found discrepancy in 9.87% of cases [30-31] Blosser et al found synchronous clinical and post mortem diagnoses in 83% of patients; the same clinical and pathologic cause of death in 66% of patients; and findings that would have changed medical ICU therapy had the findings been known in 27% patients [32]. The reason for the high number of diagnostic errors in our cases may be due to the fact that as a developing country, our diagnostic facilities fall behind that of the relatively advanced and technologically driven medical practice of the developed countries, which affords them the ability to make better diagnoses and give better care.

In the study by Zarbo et al, 40% of autopsies revealed at least one unexpected finding which contributed to the death of patients, [33] while Friederici et al reported major unexpected findings in 64% of their cases from routine postmortem examinations [34]. We consider these findings to be indeed very high, considering the. Nevertheless, it also correlates well with the findings of Komolafe etal.[7] This is however very disturbing considering the societies where the Zarbo et al and Friederici et al carried out their studies, where practice is guided by technology and is more meticulous due to the fear of litigations for medical negligence and medical malpractice. Daramola et al reported 11% discrepancies in their series in Lagos, Nigeria [35]. This falls much below our finding but it is noteworthy to state that Daramola et al conducted their study in the same environment as ours. Their very low discrepancy compared to ours may be explained by differences in hospital policies and standard practices as well as hierarchical structures of the attending personnel which may play a very crucial role in the diagnoses, case management and prognosis [7]. Komolafe et al explained the reasons for the high number of misdiagnoses in their study to be due to poor diagnostic facilities, being at variance with clinical skills in their practice environment [7]. The peculiarity of the Nigeria tertiary hospitals is allows younger physicians in training to gain experience by seeing cases before their more experienced senior colleagues such that the time wasted in bureaucracy may contribute to the undesirable morbidities and fatal outcomes[7].

In this study majority of the clinical cause of death was due to complications of systemic hypertension followed by infections, gastrointestinal/liver diseases and neoplasms. These deaths were recorded mostly in the middle-age group and the elderly with majority of the deaths seen in the male gender. The major anatomic (organ changes) findings were discovered in the brain 48.1% and gastrointestinal/liver 46.7%. This was followed by lung 43.7% and heart 32.3%. These major organs changes in lung, brain an heart were mostly observed [36] among the middle age group and then the elderly. We found the cause of death at autopsy, to be mainly

due to sequelae of systemic hypertension followed by gastrointestinal/liver diseases. Mbakwem et al[36] and Sunday et al[37] both in Lagos Nigeria in their separate studies reported intracerebral haemorrhage as the commonest cause of death discovered at autopsy which were attribute to complication arising for systemic hypertension which is similar to this study. In some other studies by Faduyile et al[38] in Lagos Nigeria and Ogeng'o et al[39] in Kenya reported acute left ventricular failure and myocardial infarction as the most prevalent cause of death discovered at autopsy respectively as a complication of hypertension. The reasons for these differences may be due to limited access to good health, inaccessibility of drugs, poor drug compliance, late presentation and the fact that patients consult alternative medical practitioners. Furthermore, it can be alluded to the fact that hypertension as the background cause in majority of cases runs a more severe course with more target organ damage in Negroid compared to Caucasians.

Some of the discrepancies are errors of judgement which may due to negligence on the part of the managing team. These include common ailments in our environment which are easily diagnosable by first principles and in fact treatable benign conditions. Failure to recognize them led to fatal outcomes. The most frequently observed major discrepancy in this study was cardiopulmonary complication, cardiovascular complications and neoplasm. This was quite different from what was found in studies by Tavora et al, [21] Kuijper et al [10] and Spiliopoulou et al [40]. They reported aneurysm, pulmonary emboli and infections as the predominant missed major discrepancies in their studies. The largest single categories of unsuspected missed diagnoses in this study were pulmonary oedema, biventricular heart failure and undiagnosed neoplasms.

Baker reported major and minor diagnostic errors in 39.7% and 17.3% respectively in his autopsy series as contributing factors to patients' deaths [41]. Britton reported undiagnosed principal cause of death in 43% of the autopsies conducted in the University Hospital in Stockholm, Sweden [42]. This very high population of missed diagnoses is quite worrisome considering the status of the hospital, the expected expertise of its personnel. David et al in a systematic review also reported that autopsies discovered 23.5% of clinically missed diagnoses involving principal or underlying cause of death as well as 9% of errors that would or could have changed positively the outcome for the patient, had the diagnoses being made antemortem and due actions taken[26]. Casali et al in their study series on the postmortem evaluation of suspected medical malpractice confirmed medical errors in 17% of cases; 50% of these were surgical mistakes during surgical procedures [43]. Madae et al in his autopsy series found that 4.24% of deaths from suspected cases of medical malpractice were due to medical errors which were otherwise treatable if recognized early and due actions taken[44]. Sonderegger-Iseli et al asserted that in 10-20% of cases, diagnostic errors constituting major unexpected discrepancies are encountered that would have changed the outcome for the patient, had they being discovered early premortem and the cases managed appropriately[45].

Komolafe et al showed that infections such as pulmonary tuberculosis, acute pyelonephritis, typhoid enteritis, pyogenic meningitis and lobar pneumonia were rampantly missed or misdiagnosed in their study series. This is further supported by Akinwusi et al, who showed that typhoid septicaemia was responsible for sudden death in 47.1% of patients, pulmonary tuberculosis in 17.7% of patients, and lobar pneumonia in 17.7% of patients [46]. Our finding is corroborated by Akinwusi et al, perhaps because we cover the same geo-political zone in our research, south west Nigeria. Our findings also showed that many missed cases of the stages and complications of systemic hypertension which eventually resulted in death. This is supported by Akinwusi et al whose study revealed that systemic hypertension-related causes accounted for 48.3% of sudden deaths [47]. It is however disturbing that many cases of systemic hypertension and its complications were missed in our environment, since it is well known that blacks are predisposed to systemic hypertension and its potentially fatal complications.

Most of the major discrepancies are found among the patients in the middle-age group and mostly in males. This deviates from the discovery by Battle et al in United States, that increasing age of patient reduces the clinician diagnostic precision suggesting that most missed diagnosis are seen in the elderly[48]. Roulson et al had reported that diagnostic errors is responsible for the incredibly high number of medical disputes and litigations and that anatomical pathologists affiliated with the Royal College of Pathologists in the United Kingdom clinical diagnostic errors as high as 75% [49]. This no doubt dwarfs the cases in findings.

Conclusion

Our study showed the pivotal role of the postmortem examination in ascertaining the correctness of diagnoses. Although many of our cases showed correct antemortem clinical diagnosis, the autopsy also revealed the missed complications or revealed new diagnoses in many cases and remains a veritable means of assessing correctness of the premortem diagnoses and a medical audit and knowledge gained would inform better practice standards that would prevent medical litigations and prevent issuance of false death certifications. Therefore, autopsies should be given its prominent place in clinical practice so that medical students and physicians in specialist training would be ingrained with the unlimited benefits of providing information crucial for medical education and improving the quality of patient's care.

Recommendation

Autopsy remains the only means of assessing discrepancies most especially in areas of infections, cardiopulmonary diagnosis and solid tumour diagnosis as well as post-surgical complication as discovered in this study. Achieving higher autopsy rate requires that the clinicians and the health care organization/management be strongly persuaded of the importance of autopsy as part of teaching, training and quality assurance programs. In this

era of personalized precision medicine, it suffices to say that a bright light is now focused on patient safety, but diagnostic errors lie in the dark and only traditional autopsy can shed sufficient light to make it visible.

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APPENDIX 1
INFORMATION FOR AUTHORS

All authors listed in a paper submitted to Asian Archives of Pathology (AAP) must have contributed substantially to the work. It is the corresponding author who takes responsibility for obtaining permission from all co-authors for the submission. When submitting the paper, the corresponding author is encouraged to indicate the specific contributions of all authors (the author statement, with signatures from all authors and percentage of each contribution can be accepted). Examples of contributions include: designed research, performed research, contributed vital new reagents or analytical tools, analysed data, and wrote the paper. An author may list more than one type of contribution, and more than one author may have contributed to the same aspect of the work.

Authors should take care to exclude overlap and duplication in papers dealing with related materials. See also paragraph on Redundant or Duplicate Publication in "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" at http://www.icmje.org/index.html.

The submitted manuscripts will be reviewed by the members of the Editorial Board or the expert reviewers. At the discretion of the Editorial Board, the manuscripts may be returned immediately without full review, if deemed not competitive or outside the realm of interests of the majority of the readership of the Journal. The decision (reject, invite revision, and accept) letter will be coming from the Editorial Board who has assumed responsibility for the manuscript's review. The editor's decision is based not just on technical merit of the work, but also on other factors such as the priority for publication and the relevance to the Journal's general readership. All papers are judged in relation to other submissions currently under consideration.

Categories of Manuscripts

1. Letters to the Editor

The letters to the editor are the reactions to any papers published in AAP. These letters will be reviewed by the Editorial Board and sent to the authors of the original paper

with an invitation to respond. Letters and eventual responses will be published together, when appropriate.

- *Word Count: 300 – 500 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figure or Table: Maximum of 1 (if needed)*

2. Original Articles

The original articles are the researches describing the novel understanding of anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal medicine or medical jurisprudence), molecular medicine or pathobiology. Systematic reviews, meta-analyses and clinical trials are classified as articles. The articles should be clearly and concisely written in the well-organised form (see ***Organisation of Manuscripts***): abstract; introduction; materials and methods; results; discussion; and conclusions. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two or more experts in the field.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Structured Abstract (see **Organisation of Manuscripts**): 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 6*

3. Review Articles

The review articles are generally invited by the Editor-in-Chief. They should focus on a topic of broad scientific interest and on recent advances. These articles are peer-reviewed before the final decision to accept or reject the manuscript for publication. Therefore, revisions may be required.

- *Word Count: 3,000 – 5,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 150*
- *Figures or Tables: Maximum of 4*

4. Case Reports

AAP limits publication of case reports to those that are truly novel, unexpected or unusual, provide new information about anatomical pathology, clinical pathology (laboratory medicine) or forensic medicine (legal medicine or medical jurisprudence). In addition, they must have educational value for the aforementioned fields. The journal will not consider case reports describing preventive or therapeutic interventions, as these generally require stronger evidence. Case reports that involve a substantial literature review should be submitted as a review article. The submitted case reports will undergo the usual peer-reviewed process.

- *Word Count: 1,200 – 2,000 words (excluding abstract, references, and figure or table legends)*
- *Unstructured Abstract: 150 – 200 words*
- *References: Maximum of 20*
- *Figures or Tables: Maximum of 4*

5. Case Illustrations

Case illustrations are aimed to provide education to readers through multidisciplinary clinicopathological discussions of interesting cases. The manuscript consists of a clinical presentation or description, laboratory investigations, discussion, final diagnosis, and up to 5 take-home messages (learning points). Regarding continuous learning through self-assessment, each of the case illustrations will contain 3 – 5 multiple choice questions (MCQs) with 4 – 5 suggested answers for each question. These MCQs are placed after the final diagnosis and the correct answers should be revealed after the references. The questions and take-home messages (learning points) are included in the total word count. The manuscripts that have passed an initial screening by the Editorial Board will be reviewed by two experts in the field.

- *Word Count: 1,000 – 2,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 10*
- *Figures: Maximum of 2*
- *Tables: Maximum of 5*

6. Technical Notes

The technical notes are brief descriptions of scientific techniques used in the anatomical pathology, clinical pathology (laboratory medicine), forensic medicine (legal

medicine or medical jurisprudence), molecular medicine or pathobiology. The submitted manuscripts are usually peer-reviewed.

- *Word Count: Maximum of 1,000 words (excluding references and figure or table legends)*
- *Abstract: Not required*
- *References: Maximum of 5*
- *Figures or Tables: Maximum of 2*

Organisation of Manuscripts

1. General Format

The manuscripts written in English language are preferable. However, Thai papers are also acceptable, but their title pages, abstracts, and keywords must contain both Thai and English. These English and Thai manuscripts are prepared in A4-sized Microsoft Word documents with leaving 2.54-cm (1-inch) margins on all sides. All documents are required to be aligned left and double-spaced throughout the entire manuscript. The text should be typed in 12-point regular Times New Roman font for English manuscript and 16-point regular TH SarabunPSK font for Thai manuscript.

The running titles of English and Thai manuscripts are placed in the top left-hand corner of each page. They cannot exceed 50 characters, including spaces between words and punctuation. For the header of English paper, the running title will be typed in all capital letters. The page number goes on the top right-hand corner.

Footnotes are not used in the manuscripts, but parenthetical statements within text are applied instead and sparingly. Abbreviations should be defined at first mention and thereafter used consistently throughout the article. The standard abbreviations for units of measure must be used in conjunction with numbers.

All studies that involve human subjects should not mention subjects' identifying information (e.g. initials) unless the information is essential for scientific purposes and the patients (or parents or guardians) give written informed consent for publication.

2. Title Page

The title page is the first page of the manuscripts and must contain the following:

- The title of the paper (not more than 150 characters, including spaces between words)
- The full names, institutional addresses, and email addresses for all authors (If authors regard it as essential to indicate that two or more co-authors are equal in status, they may be identified by an asterisk symbol with the caption "These authors contributed equally to this work" immediately under the address list.)

- The name, surname, full postal address, telephone number, facsimile number, and email address of the corresponding author who will take primary responsibility for communication with AAP.
- Conflict of interest statement (If there are no conflicts of interest for any author, the following statement should be inserted: "The authors declare that they have no conflicts of interest with the contents of this article.")

3. Abstract

A structured form of abstract is used in all Original Article manuscripts and must include the following separate sections:

- *Background: The main context of the study*
- *Objective: The main purpose of the study*
- *Materials and Methods: How the study was performed*
- *Results: The main findings*
- *Conclusions: Brief summary and potential implications*
- *Keywords: 3 – 5 words or phrases (listed in alphabetical order) representing the main content of the article*

4. Introduction

The Introduction section should clearly explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

5. Materials and Methods

The Materials and Methods section must be described in sufficient detail to allow the experiments or data collection to be reproduced by others. Common routine methods that have been published in detail elsewhere should not be described in detail. They need only be described in outline with an appropriate reference to a full description. Authors should provide the names of the manufacturers and their locations for any specifically named medical equipment and instruments, and all chemicals and drugs should be identified by their systematic and pharmaceutical names, and by their trivial

and trade names if relevant, respectively. Calculations and the statistical methods employed must be described in this section.

All studies involving animal or human subjects must abide by the rules of the appropriate Internal Review Board and the tenets of the recently revised Helsinki protocol. Hence, the manuscripts must include the name of the ethics committee that approved the study and the committee's reference number if appropriate.

6. Results

The Results section should concisely describe the findings of the study including, if appropriate, results of statistical analysis which must be presented either in the text or as tables and figures. It should follow a logical sequence. However, the description of results should not simply repeat the data that appear in tables and figures and, likewise, the same data should not be displayed in both tables and figures. Any chemical equations, structural formulas or mathematical equations should be placed between successive lines of text. The authors do not discuss the results or draw any conclusions in this section.

7. Discussion

The Discussion section should focus on the interpretation and the significance of the findings against the background of existing knowledge. The discussion should not repeat information in the results. The authors will clearly identify any aspects that are novel. In addition, there is the relation between the results and other work in the area.

8. Conclusions

The Conclusions section should state clearly the main summaries and provide an explanation of the importance and relevance of the study reported. The author will also describe some indication of the direction future research should take.

9. Acknowledgements

The Acknowledgements section should be any brief notes of thanks to the following:

- *Funding sources*
- *A person who provided purely technical help or writing assistance*
- *A department chair who provided only general support*
- *Sources of material (e.g. novel drugs) not available commercially*

Thanks to anonymous reviewers are not allowed. If you do not have anyone to acknowledge, please write "Not applicable" in this section.

10. References

The Vancouver system of referencing should be used in the manuscripts. References should be cited numerically in the order they appear in the text. The authors should identify references in text, tables, and legends by Arabic numerals in parentheses or as superscripts. Please give names of all authors and editors. The references should be numbered and listed in order of appearance in the text. The names of all authors are cited when there are six or fewer. When there are seven or more, only the first three followed by "et al." should be given. The names of journals should be abbreviated in the style used in Index Medicus (see examples below). Reference to unpublished data and personal communications should not appear in the list but should be cited in the text only (e.g. A Smith, unpubl. Data, 2000).

- *Journal article*
  1. Sibai BM. Magnesium sulfate is the ideal anticonvulsant in preeclampsia – eclampsia. Am J Obstet Gynecol 1990; 162: 1141 – 5.
- *Books*
  2. Remington JS, Swartz MN. Current Topics in Infectious Diseases, Vol 21. Boston: Blackwell Science Publication, 2001.
- *Chapter in a book*
  3. Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Bloom SL, Wenstrom KD. Hypertensive disorders in pregnancy. In: Cunningham FG, Hauth JC, Leveno KJ, Gilstrap L III, Brom SL, Wenstrom KD, eds. Williams Obstetrics, 22nd ed. New York: McGraw-Hill, 2005: 761 – 808.

11. Tables

The tables should be self-contained and complement, but without duplication, information contained in the text. They should be numbered consecutively in Arabic numerals (Table 1, Table 2, etc.). Each table should be presented on a separate page with a comprehensive but concise legend above the table. The tables should be double-spaced and vertical lines should not be used to separate the columns. The column headings should be brief, with units of measurement in parentheses. All abbreviations should be defined in footnotes. The tables and their legends and footnotes should be understandable without reference to the text. The authors should ensure that the data in the tables are consistent with those cited in the relevant places in the text, totals add up correctly, and percentages have been calculated correctly.

12. Figure Legends

The legends should be self-explanatory and typed on a separate page titled “Figure Legends”. They should incorporate definitions of any symbols used and all abbreviations and units of measurement should be explained so that the figures and their legends are understandable without reference to the text.

If the tables or figures have been published before, the authors must obtain written permission to reproduce the materials in both print and electronic formats from the copyright owner and submit them with the manuscripts. These also follow for quotes, illustrations, and other materials taken from previously published works not in the public domain. The original resources should be cited in the figure captions or table footnotes.

13. Figures

All illustrations (line drawings and photographs) are classified as figures. The figures should be numbered consecutively in Arabic numerals (Figure 1, Figure 2, etc.). They are submitted electronically along with the manuscripts. These figures should be referred to specifically in the text of the papers but should not be embedded within the text. The following information must be stated to each microscopic image: staining method, magnification (especially for electron micrograph), and numerical aperture of the objective lens. The authors are encouraged to use digital images (at least 300 d.p.i.) in .jpg or .tif formats. The use of three-dimensional histograms is strongly discouraged when the addition of these histograms gives no extra information.

14. Components

14.1. Letters to the Editor

The Letter to the Editor manuscripts consist of the following order:

- *Title Page*
- *Main Text*
- *References*
- *Table (if needed)*
- *Figure Legend (if needed)*
- *Figure (if needed)*

14.2. Original Articles

The Original Article manuscripts consist of the following order:

- *Title Page*
- *Structured Abstract*
- *Introduction*
- *Materials and Methods*
- *Results*
- *Discussion*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.3. Review Articles

The Review Article manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Main Text*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.4. Case Reports

The Case Report manuscripts consist of the following order:

- *Title Page*
- *Unstructured Abstract*
- *Introduction*
- *Case Description*
- *Discussion*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.5. Case Illustrations

The Case Illustration manuscripts consist of the following order:

- *Title Page*
- *Clinical Presentation or Description*
- *Laboratory Investigations*
- *Discussion*
- *Final Diagnosis*
- *Multiple Choice Questions (MCQs)*
- *Take-Home Messages (Learning Points)*
- *Acknowledgements*
- *References*

- *Correct Answers to MCQs*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

14.6. Technical Notes

The Technical Note manuscripts consist of the following order:

- *Title Page*
- *Introduction*
- *Main text*
- *Conclusions*
- *Acknowledgements*
- *References*
- *Table (s)*
- *Figure Legend (s)*
- *Figure (s)*

Proofreading

The authors of the accepted manuscripts will receive proofs and are responsible for proofreading and checking the entire article, including tables, figures, and references. These authors should correct only typesetting errors at this stage and may be charged for extensive alterations. Page proofs must be returned within 48 hours to avoid delays in publication.

Revised Manuscripts

In many cases, the authors will be invited to make revisions to their manuscripts. The revised manuscripts must generally be received by the Editorial Board within 3 months of the date on the decision letter or they will be considered a new submission. An extension can sometimes be negotiated with the Editorial Board.

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Step 6: Upload your manuscript file (s).

Step 7: Re-check the content of your manuscript (s) and the uploaded file (s) more carefully prior to the submission. If you have submitted your manuscript file (s) incorrectly, you must contact Editor-in-Chief of Asian Archives of Pathology immediately. The Editor-in-Chief can clear the incorrect attempt and allow you another submission.

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Assistant Professor Dr Chetana Ruangpratheep
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Editor-in-Chief of Asian Archives of Pathology

ACADEMIC MEETINGS AND CONFERENCES

Announcements of academic meetings and conferences that are of interest to the readers of Asian Archives of Pathology (AAP) should be sent to the Editor-in-Chief at least 3 months before the first day of the month of issue. The contact information is shown below.

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