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Interactive Digital Media on Mobile Platform for Teaching and Learning Neuroscience in a Medical College

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Abstract

Neuroscience has traditionally been a difficult subject to teach and learn. In an effort to ease the cognitive burden to the student when learning about the human brain, an interactive digital project was envisaged, based on the Visible Human Project of US National Library of Medicine.

It consisted of two digital sagittal images of the human head, hyperlinked to a series of sequential transverse-sliced images of the same brain at 10-20 mm intervals from the top of skull to its base, all loaded on a mobile PC-based offline platform. Copious labels, descriptive texts, explanatory notes, cross-links and on-the-fly quizzes supplemented the learning experience, besides rendering it an enjoyable interactive exercise.

Preliminary qualitative evaluations from medical students were encouraging. Non-dependency on Internet connectivity, sophisticated gadgetry or software enhanced its portability, versatility and usefulness. Comparison with eight similar digital learning media from other sources on the basis of 7 parameters confirmed the present digital project to be better than all of them, with a score of 6 on a 7-point scale.

Across the board viewers were also awed by the single-click, seamless interactivity and interconnectivity of the digital media-based project, making it an experience worth remembering by all observers.

While students can continue to learn from the project already created, definitive usability testing of the program with standardized instrument will cement its effectiveness. Furthermore, this work can be expanded to other fields of research and education which will benefit Health science students, Clinicians, Educators and Researchers in Anatomy, Radiology and Surgery.

Keywords: Interactivity, Digital media, College education, Neuroscience, Mobile platform, Standalone

1. Introduction

The Visible Human Project (VHP) of U.S. National Library of Medicine (NLM) has generated high resolution radiological and anatomical digital image dataset of a male and female human cadaver\(^1\). The cadavers were frozen, embedded in gelatin, horizontally-sliced at 1 mm (male body) and 0.33 mm (female body) intervals and digitized by the University of Colorado under NLM contract. The reconstructed data could be rotated, dissected, viewed separately in any plane and reassembled\(^2, 3\). Many organizations have licensed the dataset from NLM and created digital images of their own for educational purposes\(^4-11\).

2. Background

Explaining the structures within the human brain, with its three-dimensional voxel, is a challenge to teachers and a near-insurmountable learning curve for students. It is compounded by the inherently complex configurations of structures within the brain itself.
3. Objective and design principle

In an effort to render the learning-process user-friendly and less cognitively challenging, an interactive digital brain project was envisaged, based on the Visible Human Project dataset [1]. The design of the project was based on the human computer interface design principle embodied in Fitts' Law, which states that the time to move to a target is a function of the ratio of distance of the target and its width [12].

4. Material and methods

Horizontal lines at 10-mm intervals were drawn to scale on an MS™ Word document in Web layout view and this page was scanned as a JPEG image without resizing (Figure 1). A sagittal image model of the human head, with the brain in situ, was selected from the Visible Human Database of the NLM, scaled to the same size as the previous image, and saved as a separate JPEG image (Figure 2) [3]. This image of the brain was superimposed on the previous JPEG image in Microsoft© Paint under the same magnification and saved as a new JPEG image. This composite image contained both, 10-mm spaced horizontal lines and the sagittal image of the brain superimposed on them. The horizontal line corresponding to the scalp surface was counted as zero. All subsequent lines below were numbered according to their distance from the scalp surface in millimeters (mm). This composite 'parent' image was embedded in another Word document in same layout view and magnification as the first image. Two such files were created, designated 'A' and 'B'. 'A' showed transverse slices of the brain from 0 to 300 mm from scalp surface. The 'B' file showed similar slices from 300 to 500 mm from scalp surface (Figures 3 and 4).

Figure 1 (Left): Horizontal lines at 10-mm intervals were drawn to scale on an MS™ Word document in Web layout view and this page was scanned as a JPEG image without resizing. Figure 2 (Right): A sagittal image model of the human head, with the brain in situ, was selected from the Visible Human Database of the NLM and saved as a JPEG image with the same magnification as the Figure 1 (Image courtesy: NLM).
Figure 3 (left) and 4 (right): Both figures show the digital sagittal slice 'parent' images of the head, arbitrarily labeled 'A' (Figure 3) and 'B' (Figure 4). Horizontal lines were seen across it, labeled at 10-20 mm intervals. Figures 3 and 4 are the same image, but used separately for the upper and lower halves of head, respectively. File 'A' (Figure 3) shows transverse slices of the brain from 0 to 300 mm from scalp surface. File 'B' (Figure 4) shows similar slices from 300 to 500 mm from scalp surface (Image courtesy: NLM).

Next, multiple sequential transverse-sliced (axial) images of the brain, at 10 to 20-mm intervals from scalp surface, were obtained from the National Library of Medicine Database (Figure 5). These transverse-sliced ‘child’ images were inserted sequentially in the previous files ‘A’ and ‘B’ containing the 10-mm graduated sagittal image. Sequential transverse images of head from scalp surface to 300 mm below were embedded in file ‘A’. Sequential transverse images of head from 300 mm to 500 mm from scalp surface were embedded in file ‘B’. Each transverse image was bookmarked. Numbered horizontal lines in the sagittal ‘parent' image at 10 or 20-mm intervals were hyperlinked to correspondingly numbered transverse-sliced ‘child' images of the brain. The structures visible in each transverse image were extensively labeled. Numerous cross-links, descriptive texts, quizzes and explanatory tooltips were also added to each transverse ‘child’ image (Figures 6 to 9). Each file ‘A’ and 'B' was rendered into single-file .HTM format.

Figure 5: Multiple sequential transverse-sliced (axial) images of the brain, at 10 to 20-mm intervals from scalp surface, were obtained from the National Library of Medicine Database (Image courtesy: NLM).
**Figure 6 (left) and 7 (right):** These figures represent two sample transverse 'child' images of the head at 120 mm and 140 mm from scalp surface. Figure 6 shows labeled structures. Figure 7 shows interactive learning quizzes, in the form of hyperlinked question marks, embedded within the project. These digital transverse 'child' images were hyperlinked to their corresponding numbered horizontal line in the sagittal 'parent' image of the brain (Figures 3 and 4). The question marks in Figure 7 are hyperlinks, with explanatory cursor tips (Image courtesy: NLM).

**Figure 8 (left) and 9 (right):** These figures represent two sample transverse 'child' images of the head at 280 mm and 290 mm from scalp surface. Figure 8 shows labeled structures. The degree of complexity in this deeper sliced image of the brain is obvious. Figure 9 shows interactive learning quizzes, in the form of hyperlinked question marks, embedded within the project. These digital transverse 'child' images were hyperlinked to their corresponding numbered horizontal line in the sagittal 'parent' image of the brain (Figure 3 and 4). The question marks in Figure 9 are hyperlinks, with explanatory cursor tips (Image courtesy: NLM).

### 4.1 Method of use and interactivity

Clicking on any number on the horizontal line (corresponding to its distance from scalp surface in mm) in the sagittal 'parent' image in either file 'A' or 'B' will bring one to the transverse 'child' image of the brain at exactly that distance from scalp surface. Clicking on the 'Top' link on any transverse image will bring the user back to the same 'parent' sagittal image. Clicking on a blue label in the transverse 'child' image will bring the user to the explanatory text. Hovering the cursor over a transverse 'child' image will bring the user to the explanatory text. Clicking on a question mark on a transverse 'child' image will give the answer on a cursor tip. Clicking on it will take the user to the answer and explanatory text. Clicking on the 'Back' link will bring the user back to the original transverse 'child' image. There was complete, seamless, fluid interactivity (Figure 10).
Figure 10: Composite figure showing interactive hyperlinks and interconnectivity between various digital media. Clicking on hyperlinked number 140 or 240 (for instance) in the sagittal 'parent' image will bring one to the respective transverse 'child' image at exactly that distance from scalp surface. Clicking on the hyperlinked 'Top' button on the 'child' image will take the user back to the original sagittal 'parent' image. Clicking on hyperlinked question mark symbol next to number 6 in Self-assessment 'child' image will take one to the correct answer. Clicking on the hyperlinked 'Back' button in the Answer Section will bring the user back to source 'child' image. This is only a small demonstration. There are many more levels of interactivity in the project that can be best experienced during actual usage (Image courtesy: NLM).

5. Result

The two standalone files, operating on offline navigational browser without Internet connection, were 17.5 and 26.2 MB respectively. The .HTM files were 3.2 to 3.6 percent of the size of original files. They were easily ported on a PC or mobile device. The information imparted therein was succinctly informative. Preliminary formative qualitative evaluation feedback from medical students revealed that they found the digital media "wonderful", "easy to use", and "very helpful" for learning Neuroscience. A semi-quantitative comparison was also performed with eight other digital media from other sources.

Seven-point comparison with eight other digital learning media

The current digital project was compared with eight other digital learning media from eight other sources, on the basis of seven parameters \([4-11]\). The seven parameters were Brain views (Sagittal and Axial), Interactivity, Labeling, Animation, Java / other technology requirement, Internet requirement and Accessibility (Free vs. Paid). Each parameter was arbitrarily allotted a score of 1; presence of first four and seventh parameter scored 1 each, and their absence scored 0. For the fifth and sixth parameter the scoring was reversed because their presence was considered as a potential hindrance to learning. On the basis of this scoring system, the current digital medium scored 6 on a 7-point scale, the lost point being due to absence of animation (Table 1).
Table 1: This table gives the score of each digital medium on a 7-point scale, based on 7 parameters.

The current project scored 6 out of 7; the lost point was due to absence of animation.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Source</th>
<th>Score (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Current work</td>
<td>6 / 7 (86%)</td>
</tr>
<tr>
<td>2</td>
<td>Ecole Poly-technique[4]</td>
<td>2 / 7 (29%)</td>
</tr>
<tr>
<td>3</td>
<td>Johannes Gutenberg[5]</td>
<td>3 / 7 (43%)</td>
</tr>
<tr>
<td>4</td>
<td>NTIS[6]</td>
<td>2 / 7 (29%)</td>
</tr>
<tr>
<td>5</td>
<td>TolTech[7]</td>
<td>2 / 7 (29%)</td>
</tr>
<tr>
<td>6</td>
<td>University of Maryland[8]</td>
<td>1 / 7 (14%)</td>
</tr>
<tr>
<td>7</td>
<td>University of Michigan[9]</td>
<td>2 / 7 (29%)</td>
</tr>
<tr>
<td>8</td>
<td>Washington University[10]</td>
<td>4 / 7 (57%)</td>
</tr>
<tr>
<td>9</td>
<td>VirtusMED[11]</td>
<td>3 / 7 (43%)</td>
</tr>
</tbody>
</table>

The current digital learning media gave sagittal and multiple transverse (axial) views of the brain, which were extensively labeled. Five comparative resources gave similar views of the brain[4, 7, 9-11], but only one site gave extensive labels[5]. Five sites allowed interactivity but not as extensively as the current project did[7, 11]. The current project was freely available offline to students, while only one of the other resources was freely available[10]. The current project did not require Internet, Java or any special software for viewing. All other comparative resources, except one[6], required Internet connectivity, and all except two required Java or other special software for viewing[5, 6]. Three comparative resources had Java-based animation[4, 10, 11], while the current project had none. Table 2 gives a critical comparison of the current learning media with eight other similar resources on the basis of seven parameters.
Table 2: This table gives a comparative analysis of the current project and 8 other similar digital learning resources on the basis of 7 parameters. Axial refers to transverse-sliced views of the brain.

<table>
<thead>
<tr>
<th>Serial #</th>
<th>Source of project</th>
<th>Brain views</th>
<th>Interactivity</th>
<th>Labeling</th>
<th>Animation</th>
<th>Java / Other technology</th>
<th>Internet connectivity</th>
<th>Free Accessibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current work</td>
<td>Sagittal axial</td>
<td>Yes</td>
<td>Yes</td>
<td>Nil</td>
<td>Not needed</td>
<td>Not needed</td>
<td>Free</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Ecole Poly-technique[^4]</td>
<td>All views</td>
<td>Nil</td>
<td>Nil</td>
<td>Yes</td>
<td>Required</td>
<td>Required</td>
<td>Login required</td>
</tr>
<tr>
<td>2</td>
<td>Johannes Gutenberg[^5]</td>
<td>Axial views</td>
<td>Nil</td>
<td>Yes</td>
<td>Nil</td>
<td>Not required</td>
<td>Required</td>
<td>Paid license</td>
</tr>
<tr>
<td>3</td>
<td>NTIS[^6]</td>
<td>Axial</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Not required</td>
<td>On DVD</td>
<td>Paid license</td>
</tr>
<tr>
<td>4</td>
<td>TolTech[^7]</td>
<td>All view</td>
<td>Yes</td>
<td>Nil</td>
<td>Nil</td>
<td>Required</td>
<td>Required</td>
<td>Paid license</td>
</tr>
<tr>
<td>5</td>
<td>University of Maryland[^8]</td>
<td>Axial views</td>
<td>Yes</td>
<td>Nil</td>
<td>Nil</td>
<td>Sun workstation</td>
<td>Required</td>
<td>Licensed</td>
</tr>
<tr>
<td>6</td>
<td>University of Michigan[^9]</td>
<td>All views</td>
<td>Yes</td>
<td>Nil</td>
<td>Nil</td>
<td>Required</td>
<td>Required</td>
<td>Licensed</td>
</tr>
<tr>
<td>7</td>
<td>Washington University[^10]</td>
<td>All views</td>
<td>Yes</td>
<td>Nil</td>
<td>Yes</td>
<td>Required</td>
<td>Required</td>
<td>Free</td>
</tr>
<tr>
<td>8</td>
<td>VirtusMED[^11]</td>
<td>All views</td>
<td>Yes</td>
<td>Nil</td>
<td>Yes</td>
<td>Sophisticated devices need</td>
<td>Required</td>
<td>Licensed</td>
</tr>
</tbody>
</table>
6. Discussion

6.1 Content and context

The current digital learning media of human brain enable one to teach effortlessly, while easing the cognitive burden of the student, which is inherent in learning about the brain. It is a standalone program on offline navigational browser. It delivers the Neuroscience content in an educationally relevant manner. Bookmarks and hyperlinks within the program enable the learner to switch between sagittal and transverse (axial) image views at will. This enables easy learning of the brain structures at various depths from the scalp surface, which makes it clinically relevant, because axial images of the brain are the most frequently viewed images by clinicians and radiologists. Vivid imagery, precise labeling, interactive comprehension questions and explanatory text and cursor tips enhance students' learning. Interactivity of the program keeps their enthusiasm alive, besides allowing self-paced learning.

6.2 Learning advantages

These composite digital learning media help to ease cognitive overhead involved in learning about the human brain, enhance interest in the subject of Neuroscience, increase retention of the subject, and can provide individualized learning to cognitively-challenged learners.

6.3 Audience activities and interactivity

After witnessing a demonstration of the program first-hand, the audience will:

Get to use the program for themselves
Know about its ease of use, usability and usefulness
Experience the interactivity of the program
Get a feel of its versatility
Learn how to present a difficult subject to the learner
Vicariously feel the enthusiasm of the learner
Get to explore its applications in their own field of interest or specialization
Know about initiatives of National Library of Medicine, National Institute of Health

6.4 Future relevance

A summative quantitative usability testing needs to be done on the program, employing an instrument like the Computer System Usability Questionnaire [14]. This program can be usefully adopted by Health science students, clinicians, educators and researchers in Human anatomy, Radiology, Neurosurgery and Neurology departments. Innovators in virtual surgery research, computerized tomogram (CT) and magnetic resonance imaging (MRI) scanning can expand on this digital learning media. The current digital learning media can be rendered in 3-D with proprietary tools by anatomical image developers, for use in human-computer interaction (HCI) simulation labs.

7. Summary

The key features of the current digital learning project are; (a) Enabling effortless learning of difficult medical subject like Neuroscience; (b) Based on Cognitive domain of Bloom's taxonomy [15]; (c) Tailored to students' cognitive capacity; (d) Provision of learning feedback; (e) Complete interactivity; and (f) Availability on a standalone offline navigational browser.

Acknowledgement

Contribution from National Library of Medicine, National Institute of Health, Bethesda, Maryland is gratefully acknowledged, for making several digital images freely available on the Web for educational purposes.
References


Anomalous “Mutilated Common Trunk” Aortic Arch Embryological Basis and its Clinical Significance

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Abstract

Normally, the human Aortic arch branching into three vessels, the adult archetype of the Aortic arch and its branches are formed, due to the different growth pattern of the branchial arch arteries and their associated “migration” and “merging” of their branches. The anomalous branching patterns in the aortic arch are due to the deviations or disturbances the normal growth pattern of the aortic or branchial arch arteries during the embryonic period. The brachiocephalic trunk (BCT), the left common carotid artery (LCCA), the left vertebral artery (LVA), and the left subclavian artery (LSA) pattern was the most common four vessels arch branching pattern accounting up to 84.8%. The common trunk formation by these vessels is prevalence up to 16.1%, out of which 11% of the cases were the left vertebral artery originated with the left subclavian artery and form the “common vertebro-subclavian trunk - CVST”. The ontogenesis for these anomalous anatomical configurations and its clinical significance are still remaining unclarified. The implication of these common trunk arteries has not been properly signified in the literature till now. Till today the common vertebro-subclavian trunk Aortic arches are commonly regarded as a normal variant so, very little direct data are available. Generally, the patients with common vertebro-subclavian trunk Aortic arches are clinically normal and asymptomatic. Currently, the clinicians claimed the common vertebro-subclavian trunk Aortic arches are common in patients with atheromatic hypoperfusion and aneurysms. The present study aimed to through insight knowledge about this common trunk variant of the aortic arch. Recently, it is well identified that the suspicion exists with silent common vertebro-subclavian trunk Aortic arches, leads to sudden severe neurological complications due to the wide range of atheromatous plaques and congenital aneurysms, may cause fatal. Since the common vertebro-subclavian trunk Aortic arches are treated as “Mutilated Common Trunk –MCT” of the aortic arches.

Keywords: Mutilated Common Trunk, Common vertebro-subclavian trunk, Bovine trunk, Truncus bicuspidicus.

1. Introduction

Arch of the aorta, is the upward continuation of the Ascending aorta and it is normally branching into three vessels patterns called, the brachiocephalic trunk (BCT) or innominate artery, the left common carotid artery (LCCA) and the left subclavian artery (LSA), incidence in 74.0% - 89.4% cases in radiological investigations [1,2,3] and 63.5% to 77.3% in cadaveric studies [4,5,6]. The adult archetype of the Aortic arch and its branches are formed, due to the different growth pattern of the aortic or branchial arch arteries and their associated “migration” and “merging” of their branches [7]. The most common variance of the aortic arch was observed as the anomalous aortic arch origin of the left vertebral artery (LVA). The anomalous branching patterns in the aortic arch are due to the deviations or disturbances the normal growth pattern of the aortic or branchial arch arteries during the embryonic period.

The brachiocephalic trunk (BCT), the left common carotid artery (LCCA), the left vertebral artery (LVA), and the left subclavian artery (LSA) pattern was the most common four vessels arch branching pattern accounting up to 84.8% [8]. The common trunk formation by these arteries in the arch of the aorta was prevalence up to 16.1%, out of which 11% of the
cases were the left vertebral artery originated with the left subclavian artery [8] and form a common trunk called “common vertebro-subclavian trunk - CVST”. The ontogenesis for this anomalous anatomical configurations and its clinical significance are still remaining unclarified.

The implication of these common trunk arteries has not been properly signified in the literature till now. Till today, the CVST Aortic arches are commonly regarded as a normal variant so, very little direct data are available. Generally, the patients with common vertebro-subclavian trunk Aortic arches are clinically normal and asymptomatic. Currently, the clinicians claimed the common vertebro-subclavian trunk Aortic arches are common in patients with atheromatic hypoperfusion and aneurysms. The present study aimed to through insight knowledge about this common trunk variant of the aortic arch. The normal diameter of LVA was identified as 3-5mm, in LSA was in 10 -12mm. The vertebral artery diameter was significantly more on the left side than the opposite [9, 10, 11]. The average diameter of this common vertebro-subclavian trunk (CVST) was reported as ~ 20mm. The large diameter CVST receives the high-pressure blood from the ascending and arch of the aorta, results in the increased blood pressure in the LVA and LSA. The increased pressure in the CVST causes dilatations of LVA and LSA vessels, it may be extended up to one and a half to two times that of a normal diameter, so called as ectasia, if the dilatations occur more than the twice of the normal diameter, results in an aneurysm [12]. These aneurysms (LVA and LSA aneurysms) should be repaired to avoid possible limb and life-threatening tribulations. The increased pressure in the CVST results in the asymmetric vertebral blood flow might influence the disturbances in the cerebral arterial system, cause infarcts in the areas before or after the verteobasilar junction.

Recently, it is well identified that the suspicion exists with silent common vertebro-subclavian trunk Aortic arches, leads to sudden severe neurological complications due to the wide range of atheromatous plaques and congenital aneurysms, may cause fatal. Since the common vertebro-subclavian trunk Aortic arches are treated as “Mutilated Common Trunk – MCT” of the aortic arch.

2. Incidence

The brachiocephalic trunk, the left common carotid artery, the left VA and the left subclavian artery pattern was the most common four vessels arch branching pattern accounting up to 84.8%. The common trunk formation by these arteries in the arch of the aorta was prevalence up to 16.1%, out of which 11% of the cases were the left VA arose with the left subclavian artery [8] from a common trunk called “common vertebro-subclavian trunk - CVST”.

3. Observations

On the dissected human heart specimens with the aortic arch branches, we observed most prevalence common trunk four vessels arch branching pattern called the “common vertebro-subclavian trunk – CVST” aortic arch. The arch of the aorta shows the branching pattern like the brachiocephalic trunk, the left common carotid artery, the left vertebral artery and the left subclavian artery. The Anomalous Aortic arch origin of the left vertebral artery (LVA) with the common trunk origin of the left subclavian artery (LSA) formed the “common vertebro-subclavian trunk – CVST” (Fig-1).
Fig-1: The Anomalous Aortic arch origin of the left vertebral artery (LVA) forming the “common vertebro-subclavian trunk – CVST” with the origin of the left subclavian artery (LSA). (BCT-Brachiocephalic Trunk, LCCA- Left common carotid artery and LBV-Left Brachiocephalic vein)

After its origin, the Left subclavian artery and the first part of the left subclavian artery followed its normal course to enter the foramen transversarium of the sixth cervical vertebra. On the other hand, the right subclavian and vertebral arteries are branched out normally.

Fig-2: The development of Aortic sacs A. schematics showing the proximal part of the developing heart tube and B. During the later period, the Aortic sac shows its terminal branches called Right and Left horns.

3.1 Ontogenesis for the normal aortic arch branching pattern:

During development, in the primitive heart tube, the Truncus arteriosus (aortic sac) receives six sets (right and left) of Aortic or branchial arterial arch [13]. These arterial arches undergo selective apoptosis, and the residual branch vessels constitute the formation of Aortic arch and its great vessels. Any deviations in this normal process will result in the anatomical variance.

The first and second sets (right and left) arterial arches (I and II) are usually gets regressed. The third pair (right and left) arterial arches (III), forms the proximal part of the common carotid arteries bilaterally. The proximal part of the right fourth arterial arch (IV) persists as the right subclavian artery up to the origin of the internal thoracic (mammary) artery, whereas the distal part of the right fourth arterial arch gets regressed. The distal part of the left fourth arterial arch regresses and its proximal part forms a small segment of the adult Aortic arch between the origin of the left common carotid artery and the left subclavian arteries. The right and left, fifth arterial arch (V) either regresses or incompletely formed. The proximal part of the right and left sixth arterial arch (VI) forms the pulmonary arteries. The distal part
of the right side sixth arch (VI), becomes ductus arteriosus, whereas in the left side distal part will regress completely [14]. The right horn of the Aortic sac forms the brachiocephalic trunk (BCT) or innominate artery and the left horn of the Aortic sac, normally forms the part of the Aortic arch intervenes between the origins of the brachiocephalic trunk (BCT) or innominate artery and the left common carotid (LCCA) arteries.

Normally, the anterior part of the Truncus arteriosus receives the third (III) and fourth (IV) sets (right and left) of arterial arches; eventually, it opens into the right and left horns of the Aortic sac. The posterior part of the Truncus arteriosus receives the sixth (VI) sets (right and left) of arterial arches, and forms the right and left pulmonary arteries. The formation of the spiral or Conotruncal septum divides the Truncus arteriosus into the anterior ascending aorta and the posterior pulmonary trunk. The anterior part of the Truncus arteriosus continuous above as the Aortic sac, where it connects with the third (III) and fourth (IV) sets (right and left) of Aortic or branchial arch arteries. Ultimately, the aortic sac and its horns receive, all the derivatives of third (III) and fourth (IV) sets (right and left) of Aortic or branchial arches (Fig-2 & 3).

**Fig-3:** The derivatives of aortic arch arteries A. schematics showing the Truncus arteriosus receives the third (III) and fourth (IV) sets (right and left) of Aortic arch arteries, ultimately it is opens into the right and left horns of the Aortic sac and B. Derivatives of the Aortic sac horns and third (III) and fourth (IV) sets (right and left) of Aortic arch arteries. (BCT-Brachiocephalic trunk, RSA-Right subclavian artery, RCCA-Right Common carotid artery, LCCA-Left Common carotid artery and LSA-Right subclavian artery)

**3.2 Normal ontogenesis of left vertebral and subclavian arteries:**

The small intersegmental branches arise from the dorsal aorta, extends from the cranial (cervical) to the caudal (sacral) region, to vascularize the somites of the developing embryo. In the cervical region, these intersegmental arteries are named as C1 to C7. The vertebral artery normally developed from the cervical intersegmental arteries. The dorsal branches (distal part) from the cervical intersegmental arteries from C1 to C7 are fused to form the postcostal longitudinal anastomosis. Normally, the first part of vertebral artery developed from the distal part of the seventh cervical intersegmental artery and its (proximal part) dorsal branch (proximal to postcostal anastomosis). The sixth cervical intersegmental artery and its dorsal division are usually disappeared. The second part is derived from postcostal longitudinal anastomosis between the C6 to C1 (Fig-4 - 6). The left subclavian artery commonly developed form the proximal part of the seventh cervical intersegmental artery (Fig-4 green shaded).
**Fig-4:** Ontogenesis of normal development Aortic arch and its branches.

**Fig-5:** The schematic representation shows the Ontogenesis of: A. connections of 5th to 7th cervical intersegmental arteries with the Dorsal aorta, B. development of 1st part of left vertebral artery from the dorsal branch of 7th cervical intersegmental artery alone, and C. the 2nd part of left vertebral artery developed from the postcostal Longitudinal Anastomosis (LA) formed by the fusion of (distal segment of dorsal branches from) 6th and above cervical intersegmental arteries.

**Fig-6:** The schematic representation shows the Ontogenesis of: A. normal source of development of left vertebral artery (LVA), B. normal source of development of left subclavian artery (LSA) from the 7th cervical intersegmental artery and its branch called internal thoracic or internal mammary artery from the ventral branch of 7th cervical intersegmental artery.
3.3 Embryological basis for the “common vertebro-subclavian trunk (CVST)”:

The left sixth intersegmental artery and its dorsal branch may fail to disappear. The blood from aortic arch directly flows to the persisting sixth cervical intersegmental artery forming the aortic arch origin of the left vertebral artery. This preferential blood flows through the persisting left sixth intersegmental channel, results in diminishes the normal flow through the seventh cervical intersegmental artery (to its dorsal branch), which ultimately disappear.

The first part of the left vertebral artery derived from the sixth intersegmental artery and also from the small proximal portion of its dorsal branch. The ventral branch of the sixth intersegmental artery was disappeared completely. The second part of the left vertebral artery developed from the postcostal Longitudinal Anastomosis (LA) formed by the fusion of (distal segment of dorsal branches from) sixth and above cervical intersegmental arteries. It gives the pattern of variance left vertebral artery arises from the common trunk origin with the LSA termed as “Common vertebro-subclavian trunk - CVST” (Fig- 7 and 8).

![Fig-7](image)

**Fig-7:** The schematic representation shows the Embryological basis of: A. variants origin of 1st part of left vertebral artery from the left sixth intersegmental artery and its dorsal branch, B. Normal development of the 2nd part of left vertebral artery developed from the postcostal Longitudinal Anastomosis (LA) formed by the fusion of (distal segment of dorsal branches from) 6th and above cervical intersegmental arteries, and C. the variants Aortic arch origin of left vertebral artery from the left sixth intersegmental artery.

![Fig-8](image)

**Fig-8:** The variance left vertebral artery (LVA) arises from the common trunk origin with the LSA (green shaded), termed as “Common vertebro-subclavian trunk - CVST”. The normal source of development of left subclavian artery (LSA) from the 7th cervical intersegmental artery and its branch called internal thoracic or internal mammary artery from the ventral branch of 7th cervical intersegmental artery.
4. Discussion:

Arch of the aorta, is the upward continuation of the Ascending aorta and it is normally branching into three vessels patterns called, the brachiocephalic trunk (BCT) or innominate artery, the left common carotid artery (LCCA) and the left subclavian artery (LSA), incidence in 74.0% - 89.4% cases in radiological investigations [1,2,3] and 63.5% to 77.3% in cadaveric studies [4,5,6]. The adult archetype of the Aortic arch and its branches are formed, due to the different growth pattern of the aortic or branchial arch arteries and their associated “migration” and “merging” of their branches [7]. The most common variance of the aortic arch was observed as the anomalous aortic arch origin of the left vertebral artery (LVA). The anomalous branching patterns in the aortic arch are due to the deviations or disturbances the normal growth pattern of the aortic or branchial arch arteries during the embryonic period.

The brachiocephalic trunk left common carotid artery, left vertebral artery and left subclavian artery pattern was the most common four vessels arch branching pattern accounting up to 84.8% [8]. The common trunk formation by these arteries in the arch of the aorta was prevalence up to 16.1%, out of which 11% of the cases were the left VA arose with the left subclavian artery [8] from a common trunk called “common vertebro-subclavian trunk - CVST”. The ontogenesis for these anomalous anatomical configurations and its clinical significance are still remaining unclarified.

Normally, the anterior part of the Truncus arteriosus receives the third (III) and fourth (IV) sets (right and left) of arterial arches; eventually, it opens into the right and left horns of the Aortic sac. The posterior part of the Truncus arteriosus receives the sixth (VI) sets (right and left) of arterial arches, and forms the right and left pulmonary arteries. The formation of the spiral or Conotruncal septum divides the Truncus arteriosus into the anterior ascending aorta and the posterior pulmonary trunk. The anterior part of the Truncus arteriosus continuous above as the Aortic sac, where it connects with the third (III) and fourth (IV) sets (right and left) of Aortic or branchial arch arteries. Ultimately, the aortic sac and its horns receive, all the derivatives of third (III) and fourth (IV) sets (right and left) of Aortic or branchial arches (Fig-3 & 4).

The left sixth intersegmental artery and its dorsal branch may fail to disappear. The blood from aortic arch directly flows to the persisting sixth cervical intersegmental artery forming the aortic arch origin of the left vertebral artery. This preferential blood flows through the persisting left sixth intersegmental channel, results in diminishes the normal flow through the seventh cervical intersegmental artery (to its dorsal branch), which ultimately disappear.

The first part of the left vertebral artery derived from the sixth intersegmental artery and also from the small proximal portion of its dorsal branch. The ventral branch of the sixth intersegmental artery was disappeared completely. The second part of the left vertebral artery developed from the postcostal Longitudinal Anastomosis (LA) formed by the fusion of (distal segment of dorsal branches from) sixth and above cervical intersegmental arteries. It gives the pattern of variance left vertebral artery arises from the common trunk origin with the LSA termed as “Common vertebro-subclavian trunk - CVST” (Fig- 10 and 11).

The significance of the common trunk of the arteries has not been properly indicated in the literature till now. Till today the common vertebro-subclavian trunk Aortic arches are commonly regarded as a normal variant so, very little direct data are available. Generally, the patients with common vertebro-subclavian trunk Aortic arches are clinically normal and asymptomatic. Currently, the clinicians claimed the common vertebro-subclavian trunk Aortic arches are common in patients with atheromatous hypoperfusion and aneurysms. The present study aimed to through insight knowledge about this common trunk variant of the aortic arch.

The normal diameter of LVA was identified as 3-5mm, in LSA was in 10 -12mm. The vertebral artery diameter was significantly more on the left side than the opposite [9, 10, 11]. The average diameter of this common vertebro-subclavian trunk (CVST) was reported as ~ 20mm. The large diameter CVST receives the high-pressure blood from the ascending and arch of the aorta, results in the increased blood pressure in the LVA and LSA. The increased in the pressure of the common vertebro-subclavian trunk causes dilatations of LVA and LSA.
vessels up to the one and a half to two times that of a normal diameter, so called as ectasia, if the dilatations occur more than the twice of the normal diameter, results in an aneurysm [12]. These aneurysms (LVA and LSA aneurysms) should be repaired to avoid possible limb and life-threatening tribulations. The pressure increases in the common vertebro-subclavian trunk resulting from asymmetric vertebral blood flow might influence the disturbances in the cerebral arterial system, cause infarcts in the areas before or after the vertebrobasilar junction.

An atherosclerotic lesion was the most common (60%) cause, for an aneurysm. The arterial bifurcations are the most common site for the atheromatous plaque formations. Atheromatous plaques are developed in the crucial regions with intricate blood flow patterns with fluctuation lateral pressure on the blood vessels as in the regions such as bifurcations, bends and junctions [15, 16, 17]. The patients with the common vertebro-subclavian trunk may be asymptomatic unless it involved with the atherosclerotic lesions [18]. Angiographic studies show the extracranial atheromatous plaques with the atherosclerotic lesions are very common in the first few centimeters of the CVST, often extension into the origins of LVA and LSA. The atherosclerotic lesion in the LVA causes transient hypoperfusion leads to ischemic attacks. According to the previous observations, only 20% of strokes are due to the hemorrhagic origin. Although the hemorrhagic strokes are less common than ischemic strokes, it causes more severe lesions than the ischemic type. The ischemia is often resulting from the high blood pressure or lateral wall pressure on the blood vessels which are before now damaged by the atherosclerotic lesions.

The ischemic strokes are the more common (80%) type of all strokes. Normally, the left vertebral artery (LVA) is often larger than the right vertebral artery (RVA) [19], and the dominant vertebral artery was most frequent on the left side (69.2%). The curvature of the Basilar artery (BA) was directly opposite side of the dominant vertebral artery. The aforementioned two reasons results in the Basilar artery (BA) curvature was mainly directed to the right side. The most frequent morphological change in the Basilar artery (BA) was a C-shaped bend, followed by S-shaped, J-shaped, and no bend or straight.

Conventionally, the clinicians regarded as, the congenital variant vertebral arteries are the clinically worthless findings unless it causes the vascular insufficiencies [20, 21]. On the other hand, the recent studies confirmed that the vertebral arteries insufficiencies are the major risk factors for the posterior circulation stroke [22, 23, 24, 25]. Now it is believed, the variations or anomalies in the aortic arch arteries will lead to the increased pressure in the blood across the vessels, which in turn increases the stress in the LVA, LSA and descending thoracic aorta, leading in the development of Vertebral, Subclavian, and Thoracic Aortic Aneurysms.

5. Conclusion:

Recently, it is well identified that the suspicion exists with silent common vertebro-subclavian trunk Aortic arches, leads to sudden severe neurological complications due to the wide range of atheromatous plaques and congenital aneurysms, may cause fatal. Since the common vertebro-subclavian trunk Aortic arches are treated as “Mutilated Common Trunk – MCT” of the aortic arches.

References:

Study of the Structural Variations in Musculature of Submental Region of the Neck with Emphasis on Digastric Muscle and its Clinical Implications.

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Abstract
Anatomical variation in submental region especially the digastric muscles are common & its knowledge is important for surgical purpose. The anterior belly of the digastric muscle varies greatly in its shape and size. It is important to know the variation of the digastric muscle, as it is used as a landmark in certain surgical procedures, especially for surgeons operating in the submandibular and submental region. The digastric muscle is formed by two muscle bellies: one anterior and one posterior, joined by an intermediate tendon. It is localized in the anterior cervical region. The anterior belly divides the region between the hyoid bone & the mandible into two, a lateral (submandibular) & a medial (submental triangle). This muscle participates in deglutition & mandibular movements.

30 formalin fixed cadavers were dissected, out of which 28 suprahyoid regions showed a single anterior belly of digastric muscle bilaterally, with an average length of 4.7 cm originating from the digastric fossa of the mandible and had insertions on the intermediate tendon. Anatomical variation in the anterior belly of the digastric muscles was noted in two cadaveric specimens that showed additional muscular strips unilaterally. Knowledge of the variations of the digastric muscle may prevent complications when surgery is performed in the suprahyoid region (anterior region of the neck) or during reporting of imaging techniques of the same as well as when differentiating between cervical masses.


1. Introduction
The digastric muscle is one of the suprahyoid groups of muscles present in the upper cervical region. It is characterized by two muscle bellies that are usually a single anterior and a posterior, joined together by an intermediate tendon which is attached to the hyoid bone by a fascial pulley. The posterior belly is longer than the anterior belly and is accompanied by the stylohyoid muscle. The other three suprahyoid muscles being the geniohyoid, stylohyoid and mylohyoid, are also inserted on the hyoid bone and, together with the digastric muscle, anchor this bone against the traction of the infrahyoid muscles (Lockhart et al.)[1]. Digastric muscle stabilizes the hyoid bone in addition to assisting in jaw movements [2]. Anterior belly originates from the digastric fossa on the lower border of the mandible close to the symphysis menti. It passes downward and backward resting on the mylohyoid and is inserted into the intermediate tendon. The anterior belly may cross the midline in part and very commonly seen fused with the diaphragm oris. Posterior belly originates from the mastoid notch at the medial surface of the mastoid process of the temporal bone, and a deep groove between the mastoid process and the styloid process, called the digastric groove. It passes downward and forward between carotid triangle below and behind and the digastric triangle above and front and is inserted into the intermediate tendon. The posterior belly may be augmented by a slip from the styloid process or arise wholly from it (Williams gray) [7]. Intermediate tendon is connected to the junction of the body and greater cornu of hyoid bone by means of an
inverted “U” shaped fibrous sling of deep cervical fascia (investing layer) which anchors the tendon to the hyoid bone, with bursa intervening (Lockhart et al.,[1]).

The digastic muscle begins to form in the fourth week of embryo development from the first and second pharyngeal arch (Moore and persuad)[4]. The myoblasts originate in the fourth somitomeres reach the first pharyngeal arch (Meckel arc), thereby beginning the development of the anterior belly of the digastic muscle and the mylohyoid muscle along with the mylohyoid nerve between them and hence is supplied by nerve to mylohyoid which is a branch of mandibular division of trigeminal nerve that is the nerve of first pharyngeal arch. The posterior belly of the digastic muscle is formed from myoblasts migrating from the sixth somitomeres to the second pharyngeal arch (Reichert arc) and hence carrying the nerve of second pharyngeal arch, the facial nerve. (Drake et al.)[24]. The motor neurons controlling the anterior belly of digastic are present in trigeminal motor nucleus located in the lateral pontine reticular formation surrounded by a ring of premotor neurons. On the basis of jaw muscle innervations it has been divided into two cytoarchitectonic regions, namely dorsolateral and ventromedial. The ventromedialmotor neurons innervate jaw opening muscles and the dorsolateral subdivision controls the jaw closing muscles. This observation is based on the results of retrograde tracer injections in the muscles of mastication of various species (Mascaro MB)[23].

The digastic muscle has complex cranio-cervical dynamics; when the mandible is fixed, the digastic muscle raises the hyoid bone, and when the hyoid is fixed, the digastic muscle opens the mouth by lowering the mandible (Drake et al.,[24]). Variations in the development of pharyngeal arches can lead to malformations with a variety of clinical presentations. In the previous reported studies, variations were described in accordance with the classification of Zlabek[25], which considered the phylogenetic and ontogenetic development and the classification of Yamada[26], which enumerated six different types of variations in the anterior belly. Very recently, Fujimura et. al[20] put forward the proposition of a clear well understood classification of the anterior belly of the digastic muscle based on the positions of the attachments of the muscle bellies (Liquidation et al.)[27].

The digastic muscle is made use in plastic surgery, where the digastic anterior belly transfer technique is employed to restore the depressor function of the lower lip in lesions of the facial nerve after tumor resection (TAN, [28]; TERZIS and TZAFETTA [29].

2. Method

30 formalin fixed cadavers were dissected in the Department of Anatomy of various medical colleges of Nepal & India, out of which 28 suprahyoid regions of the cadavers showed a single anterior belly of digastic muscle bilaterally, with an average length and breadth of 4.7cm and 1.5cm respectively, originating from the digastic fossa of the mandible and had insertions on the intermediate tendon whereas two cadavers showed difference in the number of belly and attachment. The digastic muscles that presented anatomical variations were photographed using a Canon digital camera with a canon zoom lens 3*IS,6.2-18.6mm 1:2.8-4.9, and its bellies were measured using a universal pachymeter.

3. Result

Anatomical variations in the anterior belly of the digastic muscles were noted in two cadaveric specimens that showed additional muscular strips both unilaterally and bilaterally.

Case 1: Two accessory anterior bellies on left side, one is thin, placed in the middle measuring 3.9 cm in length and 0.4cm in breadth the other being thick is medial to the first one, with a length of 5.2 cm and breadth 0.7cm were observed. The medial accessory belly arises from the mylohyoid raphe and middle one from the digastic fossa. Both the bellies are inserted by joining in common with anterior belly of the digastic muscle on the intermediate tendon.
4. Discussion

There have been descriptions of anatomical variations in the digastric muscle ever since 1847[21]. Testut[19] reported variations in the anterior belly, with the presence of a supernumerary fascicle inserted in the raphe of the mylohyoid muscle, or in the hyoid bone or the digastric fossa of the opposite side. He emphasized that this variation was frequently unilateral and constituted a “trigastric” muscle.

Despite the description in the literature that unilateral variations are more frequent[22, 3], we observed the same proportions of unilateral and bilateral variations in this study. The muscle structures derived from the first pharyngeal arch, such as the anterior belly of the digastric muscle, originate from the original mesoderm of the arch[4]. Thus, deficiency in the differentiation of this layer on one side may be responsible for unilateral variations, or deficiencies on both sides for bilateral variations.

Unilateral anatomical variations may present greater clinical importance, since in some cases they may be responsible for asymmetry in the anterior region of the neck or even in the movement of the floor of the mouth[3] or the temporomandibular joint[5], and perhaps imbalance in the movement of the larynx. These types of asymmetry may lead to slight functional abnormalities or may even be confounded, in clinical examinations and in imaging.
examinations like ultrasound, tomography and magnetic resonance, with lymph nodes, benign cervical masses like thyroglossal cysts, or neoplasia.\textsuperscript{[6]}

Likewise, such conditions must be taken into consideration in surgical procedures in the neck region, especially in relation to submandibulectomy, since this muscle and its tendon are anatomical reference points during operations. The variation of the anterior belly may be double or extra slips from this belly may pass to the jaw or the raphe of the mylohyoid muscle or decussate with a similar slip on the opposite side.\textsuperscript{[7]} The frequencies of anomalies of the digastric muscle are not well known. However, several studies have demonstrated variations of the anterior bellies and the fibrous sling of the digastric muscle. An abnormal digastric muscle with unilateral quadripartition of the anterior belly was observed by Celik et al.\textsuperscript{[8]}

Sarikcioglu et al.\textsuperscript{[9]} reported an anomalous digastric muscle with three accessory bellies and one fibrous band. Anatomical variations of the anterior bellies of the digastric muscle could be significant during diagnostic and surgical procedures involving the suprathyroid region. The anatomical variations of the anterior bellies of the digastric muscle could be significant during diagnostic and surgical procedures involving the suprathyroid region. Knowledge of the muscular irregularities of the submandibular region is important because mobilization of myocutaneous flaps in reconstructive procedures is an essential element in certain plastic surgery techniques (Guelfguat et al.).\textsuperscript{[10]}

Norton\textsuperscript{[11]} reported a case of bilateral occurrence of accessory digastric muscles, which inserted upon the midline raphe, decussated, and continued to rejoin the contralateral anterior bellies of the digastric muscles before their transition into the intermediate tendons. The anomaly reported in that case was symmetrical bilaterally. Furthermore, Uzun et al.\textsuperscript{[12]} presented a case in which 3 anterior and posterior bellies of the digastric muscle had their normal origin and course and were joined by an intermediate tendon.

Holibkova and Machalek\textsuperscript{[13]} reported two anomalies of the anterior bellies of digastric muscles. Connell and Shamoun\textsuperscript{[14]} encountered excess digastric muscle bulk in several cases, observing that the large digastric muscle became apparent, bulging through the overlying platysma, when the patient was lying in the supine position with the head flexed. Aktekin et al.\textsuperscript{[15]} reported bilateral and symmetrical variation of the anterior belly of the digastric muscle. Çelik et al.\textsuperscript{[8]} reported that the anterior belly of the left digastric muscle had four separate insertions to an ipsilaterally enlarged digastric fossa.

Sargon and Çelik\textsuperscript{[16]} found a digastric muscle with three bellies on the right. Akkön and Özkuflu\textsuperscript{[17]} reported variations of the anterior belly of the digastric muscles in two cases. Their first case had two accessory bellies on both sides, both of which inserted into the right side, whereas the second case had five-segmented anterior belly. Fourteen several other studies have demonstrated variations of the anterior bellies and the fibrous sling of the digastric muscle.\textsuperscript{[18,9]}

The anatomical variations observed in this study were limited to the anterior belly, as also described in other studies (Testut\textsuperscript{[19]}; Sargon & Çelik\textsuperscript{[22]}; Andreo et al\textsuperscript{[2]}; Peker et al\textsuperscript{[3]}; Bergman et al.\textsuperscript{[21]}; Fujimura et al.\textsuperscript{[20]}; Turan-Ozdemir et al.\textsuperscript{[16]}). It is important to consider the occurrence of these variations in the digastric muscle when differentiating between cervical masses and during surgical procedures on the anterior region of the neck, especially in the submental and submandibular triangles. The accessory digastric muscle affects diagnostic imaging and therapeutic procedures in head and neck surgery and must be considered in procedures involving this area.\textsuperscript{[23]}

5. Conclusion

It is important to consider the occurrence of these variations in the digastric muscle when differentiating between cervical masses and during surgical procedures on the anterior region of the neck, especially in the submental and submandibular triangles. Knowledge of the variations is also essential because of the importance of the muscle in reconstructive technique such as in restoring the depressor function of the lower lip.

The present study shows description of anatomical variations in the anterior belly of the digastric muscle in two cadavers. This study also demonstrates a unilateral and bilateral anomaly of the anterior bellies of the digastric muscles, which is of clinical interest with
surgery or imaging of this region. Knowledge of such variations plays significant role in planning for neck surgeries and staging of tumors and hence affects diagnostic & therapeutic procedures.

References

A Study of Non Protein Nitrogenous Substances in Renal Diseases

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Abstract

Kidneys are vital organs responsible for maintenance of body fluid, salts and electrolyte concentration. Non protein nitrogen substances have an important role in renal diseases that are serious concern to human health. The present research was carried out during 2006 at SVS Medical College and Hospital, Mahabubnagar, Hyderabad, India with the objective of examining patients with renal diseases with reference to NPN parameters. Blood samples from 30 patients were subjected to analysis of Blood Urea, Serum Creatinine, Serum Uric Acid, Serum Electrolytes, Sodium, Potassium and Chloride. The statistical analysis of the above data showed that there was significant elevation of urea and creatinine levels in the cases of renal failure. The uric acid levels were also elevated when compared to the normal, the difference is not statistically significant. All cases were advised for dialysis. Urea and Creatinine levels are considered to be reliable parameters in assessment of early renal diseases.

Keywords: Acute renal failure (ARF), Chronic Renal Failure (CRF), dialysis, NPN, electrolytes.

1. Introduction

Diseases affecting the kidneys can often be detected, even in asymptomatic patients from clues derived from routine clinical and laboratory examination. Kidneys are responsible for producing urine which is used to flush away the toxins. The kidneys also maintain a healthy balance of fluids and electrolytes or salt compounds in the body. Renal failure is a serious medical condition affecting the kidney. When a person suffers from renal failure, their kidneys are not functioning properly or no longer work at all. Renal failure can be progressive diseases or a temporary one depending on cause and available treatment options. In renal failure kidneys undergo cellular death and are unable to filter waste. This dysfunction causes a buildup of toxins in the body which can affect the blood, brain and heart as well as other complications also results. Main purpose of kidneys is to filter the blood and remove waste products and excess water. They also selectively reabsorb compounds that have been filtered thus conserving essential nutrients, electrolytes, amino acids and other biomolecules. Approximately one–quarter of the cardiac output i.e. 1200 ml of blood per minute is received by the kidneys.

There are two types of Renal Failure:

1.1 Acute renal failure: This occurs suddenly and is usually initiated by underlying causes for example dehydration, infection, serious injury to the kidney or the chronic use of over dose of pain medications like Tylenol (Acetaminophen) or Advil (Ibuprofen). Acute renal failure is often reversible with no lasting damage.

1.2 Chronic renal failure: This is more serious than acute renal failure because symptoms may not appear until the kidney is extremely damaged. Chronic renal failure can be caused by other long term diseases, such as Diabetes and high blood pressure. The symptoms of renal failure include edema which is an accumulation of fluid characterized by swelling and decrease in urination other symptoms may include a general ill feeling exhaustion and headache.
A person with kidney failure can live a relatively normal life depending on the severity of kidney failure; renal function may be restored by treating the primary disease that is responsible for the damage or by treating the kidney with medication. In severe cases of renal failure, a person might require dialysis and a kidney transplant [7]. The present study is taken up to assess the severity of the disease by using biochemical parameters such as NPN substances and electrolytes which are all estimated by standard procedures [10].

The aim of this study is to analyze the biochemical profile in renal diseases in adults. Early possible detection of any abnormal biochemical parameter will help in diagnosis of renal diseases which will help in prevention of complication and permanent damage of kidney. The kidneys excrete the waste products and fluid by using the mechanism of glomerular filtration and tubular re-absorption.

There are numerous potential causes for the damage of kidneys [7].

- Decreased blood flow.
- This may occur in extremely low blood pressure caused by trauma, complicated surgery, septic shock, hemorrhage, burns or other several complicated illnesses.
- Acute tubular Necrosis. This occurs when the tissues aren’t getting enough Oxygen or when the renal artery is blocked or narrowed.
- Over exposure to heavy metals, solvents radiographic contrast materials, certain antibiotics and other medication.
- Infections such as acute pyelonephritis or septicemia.
- Urinary track obstruction- Such as narrowing of the urinary tract, tumors, kidney stones, nephrocalcinosis or enlarged prostrate.
- Severe acute nephrotic syndrome.
- Disorders of the blood such as idiopathic thrombocytopenic purpura (ITP), transfusion reaction, or other hemolytic disorders. Autoimmune disorder such as scleroderma can cause acute renal failure.

2. Materials and method

The present study is carried out in Department of Biochemistry, S.V.S Medical College. The relevant data is gathered from the Department of medicine, S.V.S medical college and hospital during the year 2006. The present study included 20 cases of renal disease and 10 normal individuals who serve as control group. They are all above 40 years. The 20 cases were selected on the basis of the vital signs like.

- Edema
- Head ache
- Vomiting
- Loss of appetite
- Swelling of face and lower limbs
- Swelling of abdomen
- Decreased urine output

2.1 Collection of sample

2.1.1 Blood: - About 5ml of blood is collected from cubital vein by vein puncture into a sterile bottle and allowed to clot. The serum is separated and used for estimation of urea, creatinine, uric acid, sodium potassium and chloride [1].

The following bio-chemical parameters [4] are estimated and compared with normal persons of the same age group (above 40 years).

- Blood Urea (Diacetyl Monoxime Method DAM)
- Serum Creatinine (Jaffè’s Alkaline Picrate)
- Serum Uric Acid (Phosphotungstic acid Method)
- Serum Electrolytes (Roche 9180 electrolyte analyzer-(ISE) Ion-selective electrode)
3. Result and discussion

The term non-protein nitrogenous in blood includes the nitrogen present in all nitrogenous substances other than protein. The total plasma nitrogen concentration is about 250-400 mg/L. NPN of whole blood is approximately 75% greater than that of plasma because of the glutathione content of erythrocytes. Catabolism of proteins and nucleic acids results in formation of NPN compounds. The principle NPN substances are amino acids, ammonia, Urea, Uric acid and Creatinine. Urea is the major NPN constituent in plasma and constitutes 45% of total NPN substances. NPN which contributes to 69%, amino acid- 20%, creatine nitrogen- 1%, creatinine nitrogen 2% and uric acid nitrogen 8% of total plasma NPN. The amount of ammonia is negligible. Increasing concentration of these substances occur as a consequence of decreased renal function.

Urea is the main end product of protein catabolism in humans. In a healthy adult the plasma urea concentration is about 20-40 mg/dl. Tubular re-absorption becomes significant at low urine flow rates. Creatine is synthesized in the kidney, liver and pancreas. Creatine is the most important substance as it plays an important role in muscular contraction. The concentration of creatinine in the blood will increase with decreased kidney function. The serum concentration of creatinine is 0.6-1.2mg/dl for males and 0.5-1.0mg/dl for females. Both serum creatinine and creatinine clearance value have been used as indices of renal function. Uric acid is the major end product of purine catabolism in humans. An average adult has total body content of about 1.2gms of uric acid which may be considered as miscible urate pool. Approximately 60% of this pool is replaced daily by formation and excretion. Mainly uric acid formation occurs in the liver. Nearly about 200-600mg of uric acid is produced and same is excreted in 24 hrs. Total body sodium is about 4000mEq and about 50% of it is in bones, 40% in extracellular fluid and 10% in soft tissues. Sodium is the major cation of extracellular fluid. Sodium pump operates in all the cells. Normal levels of Sodium in plasma is 136-145mEq/L and in cells, it is about 12mEq/L. Normal diet contains about 5-10gm of sodium as Sodium chloride. Some amount of sodium is daily excreted through urine. When urine is formed, original glomerular filtrate (175lt per day) contains 800mg/day sodium out of which 99% is reabsorbed. Out of this, 88% is reabsorbed in proximal convoluted tubules. This is an active process. Along with sodium, water is also reabsorbed. The total body potassium is about 3500mEq out of which 75% occurs in the skeletal muscle. Potassium is the major intracellular cation and maintains intracellular osmotic pressure. Potassium requirement is 3-4 g/day. Plasma potassium is 3.5-5mEq/L. The cells contain 100-120mEq/L.

Total number of cases studied was thirty, out of which ten were normal persons. The remaining twenty were suffering from Renal Disease. The age group varied from 40-60 years. The study was done in patients who are admitted in Department of Medicine. The diagnosis of Renal Disease was done by the symptoms (edema, Hypertension, Seizures, Decreased urine output and prolonged diseases DM).

The following investigations were carried out: Blood Urea, Serum Creatinine, Serum Uric Acid, Serum Electrolytes, Sodium, Potassium, and Chloride.

The cases were discussed under two groups.

a) Control subjects
b) Abnormal group

The mean values were compared with mean values of control subjects. There is an increase in Blood Urea, Creatinine and Uric acid. The mean value of Blood urea and Creatinine are significantly raised compared with control subjects.
Table 1 and 3 show the estimated levels of Non Protein Nitrogenous substances in control group. The mean and SD values of Urea, Creatinine, Uric Acid and serum Electrolyte (Sodium, Potassium and Chloride) are within normal range. Table 2 and 3 show the values of NPN substances in renal disease patients. The mean and SD values of Blood Urea, Serum Creatinine, and Uric Acid are elevated. Serum Electrolytes are not altered and Not Significant (NS).

### Table-1: Levels of different biochemical parameters in control subject

<table>
<thead>
<tr>
<th>S.NO</th>
<th>AGE</th>
<th>SEX</th>
<th>Blood Urea</th>
<th>Serum Creatinine</th>
<th>Serum Uric Acid</th>
<th>Serum Sodium</th>
<th>Serum Potassium</th>
<th>Serum Chloride</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>Male</td>
<td>38</td>
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<td>133</td>
<td>3.8</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>Male</td>
<td>30</td>
<td>0.9</td>
<td>6.2</td>
<td>136</td>
<td>4.2</td>
<td>102</td>
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<tr>
<td>3</td>
<td>55</td>
<td>Male</td>
<td>36</td>
<td>1.1</td>
<td>5.2</td>
<td>134</td>
<td>4.6</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>50</td>
<td>Female</td>
<td>18</td>
<td>0.7</td>
<td>4.8</td>
<td>137</td>
<td>3.9</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>Male</td>
<td>35</td>
<td>1.1</td>
<td>5.6</td>
<td>134</td>
<td>4.0</td>
<td>102</td>
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<tr>
<td>6</td>
<td>55</td>
<td>Female</td>
<td>46</td>
<td>1.0</td>
<td>6.2</td>
<td>136</td>
<td>5.2</td>
<td>99</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>Male</td>
<td>28</td>
<td>0.9</td>
<td>5.2</td>
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<tr>
<td>8</td>
<td>74</td>
<td>Male</td>
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<tr>
<td>9</td>
<td>45</td>
<td>Female</td>
<td>16</td>
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<td>133</td>
<td>3.6</td>
<td>95</td>
</tr>
<tr>
<td>10</td>
<td>45</td>
<td>Female</td>
<td>16</td>
<td>0.5</td>
<td>6.2</td>
<td>138</td>
<td>3.4</td>
<td>96</td>
</tr>
</tbody>
</table>

**MEAN =** 29.0 0.9 5.66 134.7 4.05 98.9

**SD =** 10.08 0.21 1.4 2.35 0.57 2.7

### Table-2: Levels of Different Biochemical Parameters in Abnormal Subjects

<table>
<thead>
<tr>
<th>S.NO</th>
<th>AGE</th>
<th>SEX</th>
<th>Blood Urea</th>
<th>Serum Creatinine</th>
<th>Serum Uric Acid</th>
<th>Serum Sodium</th>
<th>Serum Potassium</th>
<th>Serum Chloride</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>57</td>
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<td>75</td>
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</tr>
<tr>
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<td>50</td>
<td>Female</td>
<td>153</td>
<td>8.2</td>
<td>7.0</td>
<td>128</td>
<td>2.8</td>
<td>96</td>
</tr>
<tr>
<td>3</td>
<td>60</td>
<td>Male</td>
<td>92</td>
<td>3</td>
<td>9.5</td>
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<td>80</td>
</tr>
<tr>
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<td>95</td>
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<td>5.5</td>
<td>128</td>
<td>3.3</td>
<td>103</td>
</tr>
<tr>
<td>6</td>
<td>65</td>
<td>Female</td>
<td>130</td>
<td>4.7</td>
<td>4.8</td>
<td>128</td>
<td>2.9</td>
<td>98</td>
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<tr>
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<td>Male</td>
<td>65</td>
<td>2.3</td>
<td>10.6</td>
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<td>3.4</td>
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<tr>
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<td>98</td>
<td>3.0</td>
<td>6.2</td>
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<td>4.4</td>
<td>101</td>
</tr>
<tr>
<td>10</td>
<td>55</td>
<td>Female</td>
<td>74</td>
<td>2.6</td>
<td>6.1</td>
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<td>3.8</td>
<td>96</td>
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<tr>
<td>11</td>
<td>40</td>
<td>Male</td>
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<td>6.0</td>
<td>132</td>
<td>3.9</td>
<td>80</td>
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<tr>
<td>12</td>
<td>38</td>
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<td>101</td>
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<tr>
<td>13</td>
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<td>Male</td>
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<td>4.6</td>
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<tr>
<td>14</td>
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<td>223</td>
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<td>15</td>
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<td>6.4</td>
<td>135</td>
<td>4.4</td>
<td>94</td>
</tr>
</tbody>
</table>

**MEAN =** 108.8 3.14 6.88 132.35 4.22 97.8

**SD =** 47.9 2.0 1.8 32.04 1.4 6.9
In the present study, there are two groups namely control (Normal subjects) and Abnormal group (Subjects who are suffering with renal diseases). The age varies between 40–60 years in all the subjects of both groups. All the parameters like urea, creatinine, uric acid and serum electrolytes (Sodium, Potassium and Chloride) were estimated in both the groups. About 10 cases were studied in the control group who showed normal levels of all the parameters estimated, so they served good controls. 20 cases were studied under the Abnormal group out of which 6 cases suffered from Chronic Renal Failure (CRF) and the rest of them had Acute Renal Failure (ARF). Urea and Creatinine in this abnormal group showed significant elevation, uric acid showed elevated levels but the difference was not significant, Sodium, Potassium and Chloride levels were normal when compared with the control subjects. All the 20 cases (100%) showed increased levels of Urea thereby showing much significance statistically when compared with the normal group. Out of 20 cases, 17 cases (85%) showed increased levels of creatinine which showed marked significance when compared with the normal group. Out of 20 cases, only 4 cases (20%) showed much increased levels of uric acid, but mean value shows insignificance when compared with the normal group. Serum Electrolytes (Sodium, Potassium and Chloride) didn’t show any significance when compared
with the normal group. So estimation of Urea and Creatinine levels in serum are reliable indicators.

4. Conclusion

The statistical analysis of the above data showed that there was significant elevation of urea and creatinine levels in the cases of renal failure. Though the uric acid levels were also elevated when compared to the normal, the difference is not statistically significant. Serum levels of Sodium, Potassium and chloride levels showed no statistical significance when compared to the normal levels. All cases were advised for dialysis. Urea and Creatinine levels are reliable parameters in severity of renal diseases.

References

Perspectives about Human Papilloma Virus Vaccination among Parents Attending Pediatric Clinic in Trinidad

Article by Rajini Kurup¹, Reon Elder¹, Cecil Boston², Ryan Abraham¹, Kimberly Ahow¹, Kameel Mungrue¹
¹University of the West Indies, St Augustine Campus, West Indies.
²Faculty of Health Sciences, University of Guyana, Guyana, South America

Abstract

Cervical cancer is one of the common cancers among women worldwide. Despite HPV vaccination being one of the effective preventive measures, it is still not in government vaccination programs. This study aimed to assess the perspectives on HPV vaccine among parents or guardians attending hospital clinics in Trinidad.

Method: This was a cross-sectional survey among 244 parent/guardian attending pediatric clinics in Trinidad. Majority of participants were females with 54.9% and most (63.9%) of participants were in <11 age group (p<0.05). Although 40.2% parents knew of cervical cancer (p<0.05), only 28.3% were sure about correct use of the vaccine (p<0.05). A majority of 94.7% had never vaccinated themselves against cervical cancer. Only 3.3% had vaccinated the child accompanying them and 2.5% had vaccinated their other children. Mean perception score (±SD) of the study population was 5.1 (39.3% ±16.5). Majority (62.6%) of the participants scored above mean score. Individual scores for knowledge and practices showed total knowledge score ±SD of 3.4±1.7 (p<0.05) and total practice score of 1.8±0.9 (p<0.05).

Conclusion: This study highlights the limitations among selected Trinidadian parents with respect to HPV and its implication in cervical cancer. Public education on cervical cancer needs to be well addressed into the community for more acceptances of HPV vaccine and cervical cancer prevention.

Keywords: Cervical cancer, Human papillomavirus (HPV) vaccine, pediatric clinic

1. Introduction

Cervical cancer is the fourth commonest cancer among women worldwide with estimated 528,000 new cases in 2012 (Ferlay 2013). Pan American Health Organization (PAHO) reported three different studies done on Human Pappiloma Virus (HPV) in Trinidad and Tobago (Ragin et al, 2007, Andall-Brereton et al, 2011, Hosein et al, 2013). One study in 2007 investigated HPV prevalence in 310 women who attended three primary health care centers in the northern part of Trinidad. This study had HPV prevalence of 40.6% for both low-risk and high-risk HPV. In addition, 65.9% of HPV positive women were infected with high-risk HPV. The most predominant genotypes were HPV 52, 66 and 16 with 12.7%, 10.3% and 9.5% respectively. Approximately 30% of HPV positive subjects had multiple HPV infections. In Trinidad and Tobago, HPV prevalence was higher in the younger age group compared to the oldest age groups (Andall-Brereton, 2011).

Human papillomavirus (HPV) vaccines are primarily designed to prevent HPV associated cancers that typically occur years to decades after exposure to HPV 16 and 18. Three prophylactic HPV vaccines which are available against cervical cancer are bivalent, quadrivalent, and nanovalent (9-valent) vaccines. The bivalent vaccine protects against HPV 16 and 18, the most common oncogenic HPV types, which are responsible for approximately 70% of HPV-associated cervical cancers and a large proportion of other HPV related cancers (Forman et al 2011). The quadrivalent vaccine protects against HPV 16, 18, 6 and 11 which are also responsible for genital warts and respiratory papillomatosis (Lacey et al, 2006). The 9-valent vaccine also protects against HPV 6, 11, 16, 18, 31, 33, 45, 52 and 58 (Jaura et al, 2015). Routine HPV vaccination is recommended for both females and males aged 11-12
years. HPV vaccination can be started by the age of 9 years or can be given between the ages of 13-26 years for females and 13-21 years for males who did not receive the HPV vaccine previously.

In Trinidad, routine HPV vaccination of girls began in 2013. Because of the slow natural history of HPV oncogenesis, the effect of vaccination on invasive cancers will not be evident for decades. Pre-invasive cervical intraepithelial neoplasia 2 and 3 and adenocarcinoma in situ (together referred to as CIN2+), which are detected through routine screening, take less time to develop and were used as a surrogate for cervical cancer in vaccine trials. Real-world reductions in CIN2+ have been shown in countries with high vaccination coverage and catch-up programs for older persons and where it is possible to link data across population-based disease, screening, and vaccination registries (Gertig et al, 2013; Crowe et al, 2014; Baldur Felskow et al, 2014; Pollock et al, 2014).

The CDC and NIH report low uptake of the HPV vaccine for the past few years continuously with vaccination of males being significantly lower than females. Despite a slight overall increase (3%) in both 2013 and 2014, uptake of the HPV vaccine has fallen in the past few years from its initial uptake after it was approved (CDC 2015; Nelson 2015).

This study therefore aimed to assess the perspectives on HPV and HPV vaccine of parents/guardians of children visiting the pediatric clinic in Trinidad hospitals.

2. Method

A cross sectional survey of 244 parents whose children were attending pediatric clinics at different hospitals in Trinidad, on HPV, cervical cancer and HPV vaccine, was conducted in October 2015.

Several criterions were used for participation in the study.

Inclusion criteria:

1. Participant must have at least one child in order to provide information for this study.
2. Both males and females were included in this study
3. All ethnicities were invited to participate in this study
4. Participants must have been 18 years or older to participate in this study
5. Mentality stable
6. English speaking parents

2.1. Ethics approval

Ethical approval for this study was granted by the University of the West Indies Ethics Committee. Written consent from parents or guardians was obtained prior to filling out the anonymous questionnaire.

2.2 Data analysis

Data were assessed using SPSS version 21.0 and statistical analysis was conducted using the $\chi^2$ test and a p-value $\leq 0.05$ level was considered significant. Mean $\pm$ SD was used to evaluate the total scores and individual scores of participants.

3. Results

A total of 244 parents were enrolled in the study with Clinic 1 with 40.6% parents, Clinic 2 with 37.3% parents and Clinic 3 with 22.1% parents (p<0.05). Age group of participating children were $<$11, 11-12, 13-15 and 16-18 years old with 63.9%, 11.5%, 16.0%, 8.0% respectively (p<0.05). The majority (54.9%) of the participants were females than male (45.1%) (p>0.05) (Table 1).
Table 1: Demographic characteristics of participants

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>n(%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic 1</td>
<td>99 (40.6)</td>
<td></td>
</tr>
<tr>
<td>Clinic 2</td>
<td>91 (37.3)</td>
<td></td>
</tr>
<tr>
<td>Clinic 3</td>
<td>54 (22.1)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>&lt;11</td>
<td>156 (63.9)</td>
<td></td>
</tr>
<tr>
<td>11-12</td>
<td>28 (11.5)</td>
<td></td>
</tr>
<tr>
<td>13-15</td>
<td>39 (16.0)</td>
<td></td>
</tr>
<tr>
<td>16-18</td>
<td>21 (8.6)</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Male</td>
<td>110 (45.1)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>134 (54.9)</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

Perspectives of parents were assessed by asking questions on etiology, signs and symptoms transmission, treatment and management of cervical cancer. A total of 9 questions were used to assess the participants with a maximum possible score of 13. Mean score (±SD) of the perspectives for the entire study cohort was 5.1 (39.3% ±16.5). Parents scoring mean were categorized good and those scoring <5 were categorized poor. Majority (62.6%) of the participants scored above mean score. Individual scores for knowledge and practices showed total knowledge score ±SD of 3.4±1.7 (p<0.05) and total practice score of 1.8±0.9 (p<0.05). A total of 66.8% scored good knowledge and 67.2 scored good practices (Figure 1).

![Figure 1: Overall grade of participants with regard to their knowledge and practices](image)

Majorities (40.2%) of the participants were aware of the presence of vaccines, but only 28.3% were sure about the correct use of the vaccine (p<0.05). A majority (71.7%) did not know the use of vaccine. Although majority knew about the vaccine, only 3.3% of the participants had vaccinated the child visiting the clinic and less (2.5%) had vaccinated their other children (p<0.05). Almost 94.7% had never vaccinated themselves against cervical cancer.
Many (93.0%) of the participants did not know about the types of vaccines available, but only a small number (9.0%) believed that the vaccines could have side effects (p<0.05). 73.4% believed that giving the vaccine in Trinidad would be beneficial whereas 62.3% would want their child/children to get vaccinated (p<0.05). Figure 2 demonstrates the percentage of participants and their knowledge on different HPV vaccines.

4. Discussion

Trinidad and Tobago is a multi-ethnic society consisting of people mainly belonging to East Indian or African origin, as these two races are the dominant races found in the country. This study showed the knowledge, attitudes, and practices of these social groups as the questionnaires were distributed without bias almost evenly throughout the groups. Most parents had secondary school education. Trinidad and Tobago also offers free health care to its citizens, most of the participants in this study were believed to come from the middle or lower economic class, with the assumption being that upper class families will opt to visit private doctors for their children’s health rather than rely on the public health system. Most participants indicated that they had multiple offspring, with a minority stating that they only had one child.

With respect to the values obtained, it was observed that only 21% of the population was educated sufficiently about the HPV vaccination program (this was calculated as a direct result to answers given concerning the presence of the vaccine, knowledge of the virus itself, types of vaccines for HPV as well as possible side effects of the vaccine).

It was also observed that only 3.3% of parents had a child that received the vaccine with the ratio being a 1:3 male to female ratio. These results can be explained by the basic level of education among the majority of the participants partly as an extension of their middle and lower income backgrounds limiting their social and educational mobility. The results also showed that 62.3% of participants believed that the vaccine was beneficial to the country and a similar number expressed that they would like their children to receive the vaccine in the future. Though the willingness to be vaccinated is present, lack of education was identified as the limiting factor from turning desire into reality.

The results of the study mimic those of the CDC and NIH concerning the knowledge, attitudes, and practices of participants toward the vaccination program, showing no differences between the two first world countries (Trinidad & Tobago and the USA) with both countries identifying a lack of education about the vaccine being a severe limiting factor to being vaccinated (Fernandez-Expada et al, 2014).
5. Conclusion
This study has provided essential information on the perceptions of parents in Trinidad towards HPV and cervical cancer and emphasis the need for educational and interventional programs, especially targeting women to reduce the major burden imposed by cervical cancer.

References:
An Update on the Transmission, Pathogenesis, Diagnosis, Treatment and Prevention of Zika Virus Infection

Article by Dr. Pendru Raghunath

Associate Professor, Department of Microbiology, School of Medicine, Texila American University, Guyana, South America
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Abstract

Zika virus is an arthropod-borne flavivirus, related to other flaviviruses such as dengue virus, yellow fever virus, and West Nile virus. Though Zika virus was first isolated in 1947, virus remained in relative obscurity for nearly 70 years. The epidemiology of Zika virus changed since 2007 when an outbreak occurred on Yap Island of the Federated States of Micronesia. Then, Zika virus was introduced into Brazil from the Pacific Islands and spread rapidly throughout the Americas. Zika virus has infected over a million people in the countries of South and Central America. Zika virus infection generally leads to self limiting mild, febrile illness. However, many of the recent outbreaks were linked to upsurge in cases of Guillan Barré syndrome and a rise in infants born with microcephaly. Because of these complications and rapid spread of the Zika virus infections, the world health organization declared Zika fever as a public health emergency of international concern. This review describes the current understanding about the transmission, pathogenesis, clinical features, and diagnosis of Zika virus infection.

Keywords: Zika virus; pathogenesis; microcephaly; Guillan Barré syndrome

1. Introduction

Arboviruses are an important group of viruses of medical relevance due to the wide range of illnesses they cause. Zika virus is an arbovirus, related to yellow fever (YF), dengue, West Nile, and Japanese encephalitis viruses, and most closely to Spondweni virus. It is an envelope, icosahedral positive strand RNA virus belongs to the genus flavivirus and replicate mostly in intracellular compartments associated to endoplasmic reticulum and golgi complex. Zika virus was first isolated from a Rhesus macaque obtained from the Zika forest of Uganda during 1947. After its initial discovery in 1947, it was isolated on several occasions from Aedes africanus mosquitoes. For many years, it was not known whether the virus can cause human disease. A serosurvey involving residents of multiple areas of Uganda revealed that the antibodies against Zika virus are present in 6.1% of the tested population, suggesting the human infection with Zika virus. Additional serosurveys indicated a much broader geographic distribution of human infection. The first human case was reported in Nigeria in 1954 and since then sporadic cases have been reported from different regions around the globe. The epidemiology of Zika virus changed since 2007 when an outbreak occurred on Yap Island of the Federated States of Micronesia. After that several Zika virus outbreaks were reported from New Caledonia, French Polynesia, the Cook Islands, Easter Island, Vanuatu, Samoa, Brazil and several countries in the Americas. Zika virus infection generally leads to self limiting mild, febrile illness. However, many of the recent outbreaks were linked to upsurge in cases of Guillan Barré syndrome (GBS) and a rise in infants born with microcephaly. Because of these complications and rapid spread of the Zika virus infections, the world health organization declared Zika fever as a public health emergency of international concern. Hence, scientific knowledge regarding the transmission, clinical features and diagnosis of Zika virus infection is necessary to implement effective prevention and control measures.
2. Transmission

2.1 Vector-borne transmission

Zika virus is transmitted to humans by mosquito bites. Two mosquito species belonging to stegomyia subgenus of aedes — *A. aegypti* and, to a lesser extent, *A. albopictus* are responsible for nearly all known Zika virus outbreaks. Zika virus is maintained in the community through its sylvatic cycle, where the virus circulates between non-human primates and Aedes mosquitoes, and urban cycle. In Asia, a sylvatic transmission cycle has not yet been identified. Both *A. aegypti* and *A. albopictus* are daytime feeders and are widely distributed throughout the tropical and subtropical world. Very rarely Zika virus has been identified in other mosquito species, such as *A. unilineatus*, *Anopheles coustani*, and *Mansonia uniformis*; however, these species have a low potential for transmission of the virus. So far only one report suggested the presence of Zika virus in culex species, which suggests that mosquitoes in this genus have a low vectorial capacity.

2.2 Non-vector-borne transmission

Many studies now indicates that Zika virus can be transmitted from the mother to the fetus during pregnancy. Zika virus RNA has been identified in the amniotic fluid of mothers whose fetuses had cerebral anomalies as detected by ultrasonography. Brain tissue and placetas of children who were born with microcephaly and died soon after birth, as well as in tissues from miscarriages were reported to have Zika virus antigen and RNA. Zika virus infection is also transmitted by sex. In 2013, during a Zika virus outbreak in French Polynesia, a patient sought treatment for hematospermia, and replicative Zika virus could be detected from semen samples. However, the risk factors and the duration of the risk of sexual transmission have not been determined. Male population infected with Zika virus were reported to have replicating viral particles, as well as viral RNA often in high copy numbers in sperm. So far there are no reports on the transmission of Zika virus through a blood transfusion. However, during the Zika virus outbreak in French Polynesia, viral RNA was detected in 3% of donated blood samples by reverse-transcriptase polymerase chain reaction (RT-PCR). A woman who was infected with Zika virus on the day of delivery contained high titer of infective Zika viral particles in breast milk. However, there are no reports on transmission through breast milk. Serosurvey studies have detected antibodies to Zika virus in bats, goats, and rodents. However, such serological data should be interpreted carefully, since there is cross reaction between flaviviruses. Hence, there is no well-documented reservoir animal for Zika virus.

3. Pathogenesis and clinical features

Probability of Zika virus transmission is related to the volume of fluid held in the insect’s proboscis from a prior blood meal, volume of insect salivary glands, and viral replication levels. Once Zika virus enters into host, viral envelope protein binds to specific receptors such as DC-SIGN, AXL, Tyro3, and TIM-1 expressed on the susceptible cells. Zika virus infects different cell types including skin fibroblasts, epidermal keratinocytes, and skin dendritic cells. Immature dendritic cells appear to be an important initial Zika target. This interaction triggers transcriptional activation of Toll-like receptor 3 (TLR3), RIG-I, MDA5, interferon stimulated genes including OAS2, ISG15, and MX1, and beta interferon. Similar to other flaviviruses, Zika virus infection might trigger apoptosis of infected cells, thereby evading innate immune responses and increasing initial release of infectious viral particles. Zika viruses subsequently exploit autophagy to enhance replication. One study reported that treating Zika virus infected cells with 3-Methyladenine (3-MA), an inhibitor of autophagosome formation, strongly reduces viral copy numbers in infected fibroblasts. Many other studies using murine models have suggested that autophagy plays an important role in the pathogenesis of Zika-associated primary microcephaly.
Zika virus has an incubation period of 3 to 12 days\textsuperscript{29}. Among French Polynesian blood donors who tested positive for Zika virus RNA by RT-PCR, 11 (26\%) reported conjunctivitis, rash, arthralgia, or a combination of these symptoms 3 to 10 days after donation\textsuperscript{22}. Serosurvey results from Yap island indicated that only 19\% of Zika virus infected persons developed symptoms\textsuperscript{5}. Common clinical symptoms were maculopapular rash (90\% of patients), fever (65\%), arthritis or arthralgia (65\%), nonpurulent conjunctivitis (55\%), myalgia (48\%), headache (45\%), retro-orbital pain (39\%), edema (19\%), and vomiting (10\%). No patient was hospitalized during this outbreak in Yap. Similar clinical manifestations were observed in a group of pregnant women with Zika virus infection in Brazil\textsuperscript{12}. The rash is generally maculopapular and pruritic. Fever is generally low-grade and persists for short-term\textsuperscript{30}. Other rare symptoms that are associated with acute Zika virus infection include hematospermia, transient dull and metallic hearing, swelling of the hands and ankles, and subcutaneous bleeding\textsuperscript{31-33}. These clinical symptoms are usually self-limiting and may last for four to seven days\textsuperscript{34}. Other arboviruses such as Dengue and Chikungunya also produce similar symptoms, the only difference is Zika virus-induced symptoms are milder than those of others\textsuperscript{35}. Hence, it is difficult to diagnose Zika virus infection based on clinical symptoms alone.

4. Neurologic complications

Recently, Many reports suggested the association of Zika virus infection and an increase in cases of fetal abnormalities like microcephaly, hydranencephaly, ventriculomegaly, cerebral calcifications, abnormally formed or absence of brain structures, cataracts of both eyes, calcifications of eye, and hydrops fetalis during pregnancy and yet an unproven association with Guillain Barre syndrome (GBS) in adult people\textsuperscript{36-39}. All of the microcephaly cases were reported only from Brazil and outside of Brazil, no other country has reported the association of Zika virus infection and an increase in microcephaly cases. However, several countries in the Americas and Australias also reported that an increase in GBS cases coincided with Zika virus outbreaks. The association of an increase in GBS incidence with Zika virus infection is not as solid as microcephaly. Interpretation of any change in overall GBS incidence in the region attributable to Zika virus is complicated by local fluctuations in the incidence of dengue and chikungunya\textsuperscript{40}.

An Asian-lineage strain has been associated with the recent increase in microcephaly cases in Brazil. Zika virus RNA has been detected in the placenta and amniotic fluid of women with microcephalic fetuses and in the blood of microcephalic newborns suggesting that the virus can cross the placental membrane. The virus has also been identified in the brains and retinas of microcephalic fetuses. Despite accumulating clinical evidence, direct experimental evidence showing that the Zika virus causes birth defects remains absent. Very recently, Cugola and colleagues demonstrated that Zika virus infects fetuses, causing intrauterine growth restriction, including signs of microcephaly, in mice\textsuperscript{41}. They also showed that the Zika virus infects human cortical progenitor cells \textit{in vitro}, leading to an increase in cell death. The exact mechanism by which virus might cause brain malformations is also not known. To study the mechanism, Dang et al. (2016) used human embryonic stem cell-derived cerebral organoids to recapitulate early stage, first trimester fetal brain development and showed that Zika virus efficiently infects organoids and causes a decrease in overall organoid size through activation of the innate immune receptor Toll-like-Receptor 3 (TLR3)\textsuperscript{42}. During the earliest stages of foetal development, the nervous system consists of a hollow tube running along the back of the growing embryo. The inner lining of this neural tube is packed with cells radial glia, which have fine processes spanning the thickness of the tube. Microcephaly is thought to result from a depletion of these founder population of radial glia, the neural stem cells in developing brain, either through cell death or premature differentiation. Nowakowski and colleagues reported that the AXL is a candidate viral entry receptor and is highly expressed by human radial glial cells, astrocytes, endothelial cells, and microglia in developing human cortex and by progenitor cells in developing retina\textsuperscript{43}. They also proposed that Zika virus reaches the developing brain by hematogenous spread or via the cerebrospinal fluid and...
invades radial glia cells with highest AXL expression. By preferentially destroying radial glia cells, the founder cell population that generates all cortical neurons, Zika virus can produce severe microcephaly.

Though Zika virus was discovered in 1947, why a possible correlation between Zika infection, microcephaly and GBS was not detected in outbreaks prior to the 2013–2014. It is possible that in endemic areas girls are infected and become immune well before childbearing age. The recent upsurge in microcephaly cases in Brazil might be due to the availability of large susceptible population, including pregnant women. Flaviviruses can appear significantly more pathogenic when introduced into new niches and populations, but when the virus becomes established, herd immunity develops and the virulence of that particular virus will be gradually reduced. For example when West Nile virus was introduced into North America in 1999, caused very high mortality. This high virulence was associated with specific mutations that increased viral reproductive fitness in avian hosts and the North American environment. The rapid spread of chikungunya into India was the result of a single nucleotide change that promoted the adaptation of Chikungunya virus to a different mosquito vector.

An alternative hypothesis is that viral evolutionary changes such as mutations or recombination events might be responsible for the increased virulence and a new spectrum of Zika disease. Recombination events were reported to occur in different Zika viral strains. The same study also identified that a few Zika viral genes such as envelope and NS5 are under strong negative selection pressure. Hence, episodes of negative selections together with no sign of positive selection are indicative of eradication of unwanted polymorphism in genes with functional significance. One can assume that deletions that remove glycosylation sites in the envelope gene which, in turn, increase the infectivity of Zika virus and the outbreak of Zika virus is due to negative selection. The insertion of few amino acids is seen at position 441–442 in the genomic region encoding E protein. The role of those newly inserted amino acids in the virulence of Zika virus or host-virus interaction needs to be studied. Very recently, Shrinet and colleagues analysed 50 Zika virus genomes and reported the distinct amino acid variations in the structural and nonstructural proteins of all Zika virus stains responsible for 2015-2016 outbreaks. They also reported unique motifs in the untranslated regions (UTRs) of the new Zika virus strains. However, all these speculations need experimental validation.

Zika virus can be carried by a variety of Aedes mosquitoes, but the principal species responsible for the current outbreaks is thought to be A. aegypti. A. aegypti mosquitoes also serve as vectors for dengue and chikungunya viruses. In the past two decades, dengue virus has spread through areas of South America, and the seroprevalence of dengue in some Zika virus affected areas exceeds 90%. Many reports demonstrated a degree of antigenic similarity between the dengue and zika viruses. Antibody-dependent enhancement (ADE) of infection is common among Dengue virus serotypes. The recent Zika virus outbreaks are associated with neurological complications and this could be explained by the occurrence of recent outbreaks in hyper-endemic regions of Dengue virus. Very recently, using a panel of monoclonal antibodies to dengue virus, Dejnirattisai et al., 2016 reported that most antibodies that reacted to dengue virus envelope protein also reacted to Zika virus. Using human myeloid cell line U937, they demonstrated that those antibodies were able to bind Zika virus but were unable to neutralize the virus and instead promoted ADE. Hence, immunity to dengue virus might enhance replication of Zika virus and play an important role in pathogenesis and disease outcome in Zika infection.

The exceptional climatic conditions, arising from the strong El Niño event in 2015, in northeastern South America might have contributed to the rapid dispersal of Zika virus. Recently, a study revealed that Zika virus and man have a peptide in common, hence this may be the reason for microcephaly and GBS. Along with the Zika virus, there could be other associated risk factors/agents responsible for microcephaly. Nogueira and colleagues analyzed protein extracts of three Zika positive brains by shotgun mass spectrometry and reported the presence of peptide(s) from the polyprotein of a Bovine-like viral diarrhea virus.
They hypothesized that Zika virus may not be the only etiological agent responsible for microcephaly. However, BVDV is not known to cause disease or even infection in humans. It is also a known contaminant in many cell culture reagents. Of the 25 identifications of BVDV derived peptides, 24 turned out to be identical to human proteins, many from the ubiquitin-family. Hence, their findings are of doubtful significance and needs experimental validation.

5. Diagnosis

Zika virus infection can be diagnosed based upon clinical symptoms, the prevalence of vector in the region, and by serological and molecular detection assays. The Zika virus can be isolated from mosquitoes and different samples of patients using animal inoculation and cell lines. However, isolation is less frequently employed for diagnosis because it requires long time, laborious and less sensitive because of low level of viremia. Zika virus infections are routinely diagnosed by the detection of viral nucleic acid using RT-PCR and the detection of IgM antibodies by IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA). The detection of viral RNA in serum provides a definitive diagnosis; however, in most instances viremia is transient, and diagnosis by RT-PCR has been most successful within 1 week after the onset of clinical illness. Zika virus RNA can also be detected in various other samples such as umbilical cord sample of infants, urine, nasopharyngeal swab, saliva, amniotic fluid, CSF, and frozen and fixed placenta. Persistence of Zika virus in various samples is inconsistent hence, shedding of virus in different body fluids has to be elucidated to establish a better diagnostic method combined with exact sample of choice. A report suggests that Zika virus is present in urine for more than 15 days after the onset of symptoms: if verified, this would extend the period during which a definitive diagnosis of Zika virus infection can be established by RT-PCR. Another study has compared RT-PCR results in serum and saliva samples. The study results suggested that RT-PCR had higher sensitivity in saliva than in serum. However, samples from some patients were positive in serum but not saliva, and testing of saliva samples did not extend the duration of viral RNA detection after the onset of illness. ELISA based methods can be used to detect Zika virus infection during the first week of illness, if they target virus specific antigens. Very recently, BioFront Technologies Inc. has developed the MonoTrace Zika Virus NS1 ELISA kit for specific detection of Zika virus non-structural 1 (NS1) protein. They also reported that the assay demonstrates strong reactivity to all major Zika virus genotypes yet shows no cross-reactivity with Dengue virus NS1.

IgM antibodies to Zika virus will appear as viremia wanes within the first week after symptoms onset and will persist for several months. Hence, for sera samples RT-PCR is useful within the first week of clinical illness and MAC-ELISA will be useful after first week of clinical illness. Hence, combination of RT-PCR and MAC-ELISA is likely to have the highest diagnostic yield. The considerable cross-reactivity between members of flaviviruses hinders the use of serological techniques for diagnosis of Zika infection. For example, dengue infection may also evoke a positive MAC-ELISA for Zika virus. The plaque reduction neutralization test (PRNT), the most specific test used to differentiate antibodies of closely related viruses, can be used to verify MAC-ELISA results. However, this test is labor-intensive and costly, involves handling of live virus, takes up to a week to perform, requires standardized reagents that often are not available, and is not widely performed. In settings, where PRNT is not available, specimens that are found positive by Zika virus MAC-ELISA and negative by dengue MAC-ELISA may be interpreted as a presumptive recent Zika virus infection. However, the diagnostic accuracy of this approach needs to be validated.

Reliable testing regimens for the diagnosis of prenatal and antenatal Zika virus infection have not been established. Congenital Zika virus infection can be diagnosed by screening the amniotic fluid for Zika virus RNA by RT-PCR. However, the sensitivity of RT-PCR in this context is not established. At the time of delivery, cord blood can be tested by RT-PCR and MAC-ELISA, but the sensitivities of these tests for detecting prenatal Zika virus infection
Zika virus infection in tissues of fetal losses and full-term infants who died shortly after birth can be diagnosed by RT-PCR and immunohistochemical testing\(^{18,65}\). Microcephaly is detected by measuring occipitofrontal circumference as suggested by standard charts (WHO, 2006). Ultrasonography can be employed for detection of microcephaly in pregnant women\(^{66}\). Although microcephaly and other fetal abnormalities may be detected as early as 18 to 20 weeks of gestation, they are often not detected until later in pregnancy. Furthermore, the use of ultrasonography to detect microcephaly is dependent on clinical and technical factors, and ultrasonography is not highly sensitive for detection of microcephaly. Results of ultrasonography can be verified using molecular and serological tests\(^{65}\). Molecular diagnosis involves detecting of viral RNA by RT-PCR. Blood picture reveals neutropenia and thrombocytopenia\(^{66}\).

6. Treatment

Currently, there is no specific antiviral drug available to treat Zika virus infections. Similar to other mosquito-borne flaviviruses, treatment for uncomplicated Zika virus infection focuses on symptoms. Only supportive treatment such as use of fluids, and analgesics to reduce pain and antipyretics to reduce fever is in use to treat Zika infections. Xiyanping is a semi-synthetic component extracted from Andrographis paniculata, a Chinese herb, possesses anti-inflammatory and antiviral activity\(^{67,68}\). Very recently, there is a report from China on the use of Xiyanping injection combined with supportive therapy with promising results\(^{69}\). As of now, not much attention has been given to explore new therapeutic regimens for treating Zika infection. Hence, there is a dire need to find out the suitable antiviral drug for prevention and control of Zika virus. Considering the public health significance of this virus and global concerns, future studies should concentrate on exploiting valuable therapeutic options of novel and emerging/upcoming regimens such as cytokines, RNA polymerase inhibitors, microRNA (mi-RNAs), small interfering RNA (si-RNA), probiotics, herbs/plant extracts, nutritional immunomodulation.

7. Prevention and control strategies

Currently there is no vaccine exists to counter the Zika virus infection. Though Zika virus is known since 1947, only after the recent outbreaks, the virus has assumed great significance and efforts are being made towards developing a vaccine. As many as 23 groups from different countries are working on the development of vaccine against Zika virus\(^{70}\). Since, there is no vaccine, prevention and control of Zika virus are mainly aimed at prevention of vector population (mosquitoes) as they play an important role in the transmission of this virus. These vectors can be controlled either by mechanical, chemical, and biological measures. Mechanical control methods involve removal of any objects that helps in unwanted storage of water in the premises that serve as a breeding point for female mosquitoes. Chemical control of insects and vectors can be used with caution as it can cause toxicity to animals\(^{71}\). The major disadvantage in the use of this method is the problem of resistance development and also these compounds are toxic to higher mammals thereby questioning its use for the control of vectors\(^{7}\).

As part of biological control measures, bacteria such as *Bacillus thuringiensis israelensis* can be used for mosquito control\(^{72}\). A report suggests that a fungi named *Beauveria bassiana* can also be used to control Aedes mosquitoes\(^{73}\). Another approach is the use of larvivorous fishes (e.g. *Gambusia affinis*) in the water-logging areas and flower pots which can eliminate larvae of mosquitoes\(^{74}\). Lately, the use of microbes to control vector population gained interest. For example, a bacteria named Asaia has been explored for its ability to colonize the gut and reproductive tract of mosquitoes and also to get transmitted vertically to its progeny\(^{75}\). Another bacterium named Wolbachia has the potential to feminize male vectors thereby preventing the reproduction of vectors hence controlling their population\(^{76}\). Other techniques such as irradiation have been used to generate sterile males to control the mosquito population\(^{77}\).
Apart from vector control, proper surveillance and monitoring has to be carried out at the highest level in countries where there are reports and also countries adjoining them. All international airports, harbors, and places of international tourist attraction is needed to be under the scanner for the screening of this important disease. Spread of Zika infection to pregnant women can be prevented by avoiding unnecessary travel to areas of ongoing Zika virus transmission, avoiding unprotected sexual contact with partners who are at risk for Zika virus infection, and using mosquito repellent, permethrin treatment for clothing, bed nets, and window screens.

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BBRIICCSS Online Teaching & Learning Model

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Abstract

As the world is experiencing the paradigm shift from the brick and mortar model of education to the online teaching learning model, there needs to be an online teaching learning pedagogy which blends the conventional and the current technology for an effective delivery of online courses. To this effect the BBRIICCSS online teaching learning model was created. BBRIICCSS is a uniquely designed teaching learning model designed for distance and online learning programs of Texila American University Ltd [TAU] – Hong Kong. BBRIICCSS model was used to deliver the online masters and PhD program across five schools in an effort to identify the most effective methods to deliver online courses. To gauge the effectiveness of this model an assessment was done to estimate the students learning outcome and satisfaction. Feedback from 160 students were collected from different schools of Texila American University and the results shows, 87% learning outcome, 97% professional advancement and 93% would recommend others to study in TAU. This model will facilitate in building capacities to deliver quality and effective online courses for the nascent and as well full-fledged institutions delivering online courses as well as blended learning programs

Keywords: BBRIICCSS, Contextual project work, RALO

1. Introduction

The education system is ever dynamic and worldwide institutions are gearing up themselves towards online teaching learning methods, but the question here is, do they have a proven model to deliver this online courses. In an effort to build capacities and a sustainable model, TAU has developed BBRIICCSS online teaching learning pedagogy

1.1 Defining BBRIICCSS

BBRIICCSS (BRICS) is a uniquely designed teaching learning methodology designed for the distance and online learning program where students will learn the subjects in blocks. Block based learning is dedicated learning of one subject at a time, which focuses on more immersed learning. Each block is for 2 months or 8 weeks

During the block based learning students undergo various teaching learning activities in sequence. They are expected to complete 2 modules in a week and as well as take two assessments, participate in forum on weekly basis, participate in faculty student’s interactive session, do a contextual project work during the seventh week, all these make learning comprehensive. At the end of every block, student will do a self-reflective assessment to understand if he has achieved the learning outcome of the subject.

1.2 BBRIICCSS Principles

The BBRIICCSS model is developed based on the following principles.
2. Methods

2.1 BBRRIICCSS - Process

BBRRIICCSS is the acronym of the process adopted in the online teaching learning model which is detailed below

- **B = Bringing Education to Life**, the model envisions to achieve the motto of the university
- **B = Block Based Learning** – This indicates that at a given time student does dedicated learning of one subject at a time, focuses on more immersed learning
- **R = Reflective Assessment of Learning Outcome [RALO]**, at the end of every block, student will do a self reflective assessment to understand if he has achieved the learning outcome of the subject
- **R = Research oriented learning**, the model emphasis on 2 article reviews and one original research publication, and participation in the e-conferences as a mandatory requirement
- **I = Interactive learning** – the model emphasis on faculty students interaction session, and as well as participation in the forum with their peers. Students are also required to take part in course wiki which encourages group activity
- **I = Internet based learning** - the learning activity happens through the Learning Management System and in every block students are expected to read stipulated number of PPT'S, observe video classes, review open courseware, pdf files and attend classes through WIZIQ.
- **C = Contextual Project Work [CPW]**, a student is expected to do at least one CPW per block, this gives an opportunity to the students to relate what is being taught into the context of the real world, and thus eliminating the questions of "Why do I need to learn this stuff?"
- **C = Capstone Project**, promote integrated learning and understand the connections between various subjects, which is carried out after every three blocks
- **S = Supervised Learning**, a student is provided with Faculty Support, Teaching Assistant Volunteer (TAV) support, Academic and Student Coordinators support. This facilitates constant academic support and guidance throughout the study period
- **S = Summative and Continuous assessments**, the student is subject to continuous online quizzes [minimum of 12 set of quizzes per block], final term exams and project work viva voce.

2.2 BBRRIICCSS implementation

This model was used across five different schools like School of Management, Public Health, Nursing, Clinical Research and Behavioural Sciences. Prior to implementation all the faculty members, academic coordinators, student coordinators and the students were trained.
in this model. Overall 400 students were involved in the program. The Learning Management System was also customized to suit the BBRRIICCSS mode of delivery.

3. Results

To assess the effectiveness of the BBRRIICCSS model a study was conducted and 160 students participated in the study. They had undergone courses in different subjects from five different schools. All the five schools followed the BBRRIICCSS model. Few of the questions extracted out of the set of questionnaire and the feedback obtained from the 160 students are given below.

Table 1: Knowledge and skills obtained, enabled professional advancement

<table>
<thead>
<tr>
<th>Questions</th>
<th>Excellent %</th>
<th>Very Good %</th>
<th>Others %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Course description and objectives aligned with the course content</td>
<td>36</td>
<td>57</td>
<td>7</td>
</tr>
<tr>
<td>Course content, material and activities are relevant, up to date and as per expectation</td>
<td>32</td>
<td>57</td>
<td>11</td>
</tr>
<tr>
<td>Knowledge and skills obtained, enabled professional advancement</td>
<td>46</td>
<td>51</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 1 shows that 97% of the students have rated very good and excellent against knowledge and skills obtained enabled professional advancement, which is a significant and that is one of the objectives of formal education.

Table 2: Probability of recommending TAU to others

<table>
<thead>
<tr>
<th>Questions</th>
<th>Excellent %</th>
<th>Very Good %</th>
<th>Others %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goals achieved or likely to achieve due to this course</td>
<td>39</td>
<td>57</td>
<td>4</td>
</tr>
<tr>
<td>Probability of recommending TAU to others</td>
<td>53</td>
<td>40</td>
<td>7</td>
</tr>
</tbody>
</table>

Table 2 depicts 93% under excellent and very good category in recommending TAU to others which significant and envious proposition to receive referrals.

Table 3: Reflective Assessment of Learning Outcome [RALO]

<table>
<thead>
<tr>
<th>Schools</th>
<th>Quantified learning outcome in %</th>
</tr>
</thead>
<tbody>
<tr>
<td>School of Clinical Research</td>
<td>92</td>
</tr>
<tr>
<td>School of Behavioral Sciences</td>
<td>86</td>
</tr>
<tr>
<td>School of Nursing</td>
<td>85</td>
</tr>
<tr>
<td>School of Public Health</td>
<td>87</td>
</tr>
<tr>
<td>School of Business Management</td>
<td>85</td>
</tr>
<tr>
<td>Average</td>
<td>87 %</td>
</tr>
</tbody>
</table>

RALO is a self-assessment done by the student's based on their perception about the fulfilment of the Learning Outcome. Table 3 depicts that students have quantified their learning outcome and it shows 87% on an average across five schools.

4. Discussion & conclusion

In the pursuit of identifying a suitable online teaching learning pedagogy, TAU has developed BBRRIICCSS model.
Texila American University adopting BBRRIICCSS teaching learning model has the envious number [95%] of student’s retention rate, and 87% or more learning outcome and above all 93% students are willing to refer their friends to study in TAU.

There are not very many teaching learning models for the online universities and BBRRIICCSS Model will be a boon to all those new universities and as well as established Universities.

As mentioned earlier this model is complete blend of technology and teaching learning pedagogy which would suit all types of universities offering online courses and blended learning program

5. Suggestions

Further study on different variables of BRICS and it correlation to the learning outcome will be interesting to understand.

Use of some of these techniques in Basic Medical Sciences Department of TAU – College of Medicine will improvise the teaching learning methods

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