

Organ Transplantation from Deceased Donor: Myths and Facts in Pakistan and World Over.

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Abstract:

Organ transplantation is remarkable scientific achievement in treatment of patients with end stage organ failure. Renal transplant was first solid organ transplant performed in early 50s. Initially only transplant from living donors were performed but later keeping in view of number of patients suffering from end stage organ failure and shortage of living donors, practice of retrieving organs from dead has been adopted. Such donors previously called 'cadaver' and now labelled as 'deceased' donors can be non-heart beating donors or donors with circulatory failure or could be brain dead donors. This article highlights types of organs which can be harvested from deceased donors. The ethical dimensions (which covers social, cultural, legal, religious and ethical issues) of deceased organ donation and their impact. Verdicts from religious point of view of different world religions is referred at end of article as consideration of religion cannot be denied in field of transplantation. This article also highlights definition and diagnosis of brain death, conditions necessary to fulfil retrieving organs from brain death and the ethical dimensions (which covers social, cultural, legal, religious and ethical issues) of organ donation from brain dead.

Key Words: Organ Transplantation, Brain Death, Deceased Donors, Ethical, Socio- Cultural, Religion

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Introduction:

There is huge number of patients with end stage organ failure in need of organ transplantation worldwide. The number on waiting list and time duration on waiting is on rise continuously. Several measures have been adopted world over to cut down this number on waiting list and duration. Since the inception of solid organ transplant in early 50s initially only source was live donor transplant thus only limited organs could be transplanted in those times and outcomes were not up to marked satisfaction in field of transplantation. With passage of time drastic changes in immunosuppression, methods of HLA matching and lymphocyte cross match methodologies long term outcome of organ transplant improved much. The development in science of immunosuppression has established possibility of deceased organ transplant as an important form of treatment especially for organ which cannot be taken from live donors. While limited organs can be taken from healthy living donors, deceased (previously called cadaver) organ donation requires retrieval of vital organs quickly after death. These organs become unsuitable for transplantation if retrieval is delayed thus deceased organ donor desired to be in hospital intensive care unit on mechanical ventilation at time of death.

Deceased donors can be non-heart beating donors or brain dead donors. Brain death is now established criteria for death but in certain situations relatives of dead person do not accept this while looking at electric activity of heart on monitor, as dying person is on mechanical ventilation in an intensive care setting. In these circumstances organs are retrieved (with permission of family) after heart stops and these are called as non-heart beating donors or the circulatory death of a person. Such donors are shifted to operating room for retrieval of organs immediately

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after stopping of heart as not many organs may be useful if the process is delayed. All prerequisites are made after the understanding between healthcare team and family of dying person. In all cases the family can override the will/ decision of dying person and is respected by physicians.

The term 'brain death' was introduced in 1965 after a report of renal transplant from brain dead but heart beating donor. Its formal definition was laid later in 1968¹. By definition Brain Death is cessation of cerebral function when proximate cause is known and is irreversible². The American Society of Neurology has defined brain death with three cardinal signs, that are cessation of function of brain including brain stem, coma and apnea³. Before going for diagnosing brain death following must be fulfilled:

- ✓ To determine the cause of unresponsive state that is incompatible with life which may result from major trauma or intracranial bleed with midline shift, neurological imaging like CT Scan, MRI or MRA are done.
- ✓ Then there should be exclusion of associated co-morbid which may cause unresponsiveness is a must, this include severe metabolic, electrolyte or acid base disorders.
- ✓ Then use of drugs which may cause unresponsiveness must be excluded, this includes sedatives, narcotics, muscle relaxant.
- ✓ Then core temperature should be $>32^{\circ} C^2$

Tests performed from brain death include:

- ✓ To check unresponsiveness supra orbital or pressure on nail bed is applied before proceeding for other brain stem check for reflexes.
- ✓ Absent pupillary light reflex; which tests afferent II and efferent III cranial nerves.
- ✓ Absent corneal reflex; which tests afferent V and efferent VII cranial nerves.
- ✓ Absent reflexes on face and maxillary regions; which tests V cranial nerve.
- ✓ Absent oculo-cephalic reflex (doll's eye movements, movement of neck in lateral 90° causes deviation of eyes in opposite direction); which tests afferent VIII cranial nerve.
- ✓ Absent oculo- vestibular reflex, with patient at 300 head up position when lateral semicircular canals become vertical, 50 ml of ice cold saline is injected in ear nystagmus occurs with intact reflex. This tests afferent VIII and efferent III and VI cranial nerves.
- ✓ Absent pharyngeal (gag) reflex and laryngeal (cough) reflex; which test afferent IX and efferent X cranial nerves.
- ✓ Apnea test; which is aimed to test integrity of respiratory center present in brain stem. This test is performed by disconnecting ventilator and giving oxygen at 6 L/min through a catheter placed at level of carina. Expected rise in Pa CO₂ is 3 mmHg/min so in 8-10 minutes there should be rise of 24 mmHG from base line after 10 minutes of this test. This test is considered positive with absence of respiratory movements at a PaCO₂ of 60 or 20 mmHg rise from baseline⁴. Before performing apnea test patient should have normal core temperature, normal blood pressure, off sedative and paralytic drugs, oxygen saturation of PaO₂ >200 mmHG after 100 % oxygenation and PaCO₂ between 35-45 mmHG.
- ✓ Other tests include documentation of cerebral blood flow, digital angiography is gold standard to assess cerebral blood flow, absence of intracerebral filling at the level of carotid bifurcation or vertebral arteries, confirms diagnosis of brain death. Another alternative is CT Angiography^{4,5}.
- ✓ Transcranial Doppler is also used in intensive care units; absence of diastolic biphasic flow on Doppler is diagnostic of brain stem death but test is highly operator dependent⁶.
- ✓ Electro encephalography (EEG) is also used to document brain death. An isoelectric recording from 18-20 channels for 30 minutes is suggestive, but use of sedative in patients on ventilator support may impact the results.
- ✓ Cerebral tissue perfusion with use of technetium 99 hexamethylpropylene amine oxime has also been reported for diagnosis of brain death⁷.

Therefore; considering a brain dead person for organ donation this person should be in well-equipped intensive care unit, on mechanical ventilator support, a well-trained intensive care unit staff and available trained neurologist who can perform these tests and confirm brain stem death. However, neurologist have to repeat all tests with an interval of 24 hours before announcing patient as brain dead.

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There are multiple organs and tissues which can be retrieved and used for transplantation; organs in patients with end organ failure and tissue in patients with severe handicapped or disfigured persons. These include organs like two kidneys, two lungs, two livers (with split), one heart, pancreas, stomach, part of intestine, uterus and testicles. The tissues which can be transplanted are two corneas, skin, fascia, cartilage, bone, joints etc. Composite transplant of hand and face has also been already performed⁸.

Ethical Dimensions:

Scarcity of organs requires clear and transparent criteria for determining eligibility for transplant; multidisciplinary team is required to assess eligibility of recipient. Next come assessment of suitability of available donor organs, another field which desires expertise of multidisciplinary team.

Deceased donor organ usually taken from person who was previous in good health and landed up in some intensive care setting after accidents, trauma or sudden loss of consciousness, diagnosis of brain death is made by neurologist and interventionist and then consideration for organ donation comes. This brain dead person must have made an altruistic free will, without any coercion and family or next of kin already aware of wishes of dead person. People usually sign donor cards or in some countries there is an option on driving license, donor's right of self-determination should be fully respected. Sometimes there is only verbal expression of wishes which family respects after death, while in other family denies the wishes and refuse to donate organs of their loved ones this happens more frequently than the earlier situation. Interventionist and ICU staff who are not well trained for the situation find difficulty in approaching grieving family and convince them to follow wishes of dead person. Encouragement of family members to permit organ retrieval without being coercive is tricky. Many of health care professionals in intensive care unit or emergency unit find it difficult to approach the grieving families especially if they are not well trained in this particular field. Another fact is that these staff members are busier in management of other sick patients in intensive care unit and they feel priority of giving time to patient where there is chance of saving the patient so unintentionally their efforts are more diverted towards them. There are very few facilities which have designated staff to care about brain dead patients and at same time co-ordinate with families of such patient and make it practical to save and retrieve organs for transplant without being coercive.

In countries where opt out system is followed, which means if person has not opted it out, that he or she does not want to donate organ; they are considered as potential donors and in cases of death in ICU, treating physicians are legally authorised to call organ retrieval team and all organs are supposed to be used for transplant unless objected by family. England, Wales, Austria, Belgium and Spain are examples of such countries. Highest rate of deceased organ transplant has been reported from Spain⁹.

Some relevant ethical issues with organ donation are respect for persons and their autonomous choices, balance between probable benefits against probable harms, equal distribution of risks, benefits, cost and burdens, sufficient evidence to guide in decision making and confidence in treating physicians. Trust in public can be improved with transparency and efficient provision of health care facility to common men. Also implication of law at various stages of treatment is basis of developing confidence in public. In some societies even if dying person had made a clear wish to donate organs, next of kin does not allow to do so and they bring several arguments. Mostly these are social taboos, they claim that it would go against religion. Although almost all religions at supreme level have allowed organ transplant from deceased, the common men will get information and permission from nearby available so called religious leader, who himself has not enough knowledge of religious laws and as result they draw back from donating organs of their dying relative. From ethical perspective genuine informed consent from grieving family and respect for autonomy of dying person both are equally considered.

From legal point of view, it is mandatory to have permission to retrieve organs for purpose of transplant. The first cadaveric kidney transplant was performed in Boston USA in 1962, but UK parliament rejected bill for cadaveric transplant in 1968, however UK's first heart transplant was performed during same year¹⁰. The European Council passed a resolution concerning the legalisation of organ removal and transplantation in all

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member countries in 1978¹¹. This indicates that there were countries where deceased organ transplant was performed for years without proper state laid legal framework. Legislation not only provides legal permission but prevents any potential to go beyond limits. Then question arises that what is best or ideal law for transplantation? Probably best is when law considers norm of society and cultural and religious beliefs of residents of country where this law is applied, it should not be coercive.

Organ procurement from prisoners:

In China 97% of organ transplantation are from deceased source, it was mainly possible after 1984 Regulation about use of organs from condemned criminal getting life sentence. This practice gives rise highly controversial ethical debate, while some would say that these organs can address the concern about shortage of organ to some extent and organs will anyway be going to waste. Others would argue that under these circumstances death sentence is seen as means to address organ shortage and may affect the noble cause of organ donation and judicial system, it would hurt primary altruistic philosophy and can place transplant team to be seen as executioner. Also any practice as soon as plotted as law becomes coercive.

For Brain dead donor transplant once a diagnosis of brain death has been established a person can be considered as organ donor.

It has been always difficult to accept death of loved one and in a scenario when patient is on mechanical ventilator support and heart is beating, the family could see tracing of heart beat on monitor and moving of chest wall with respiration as patient is on ventilator, convincing the loved ones that their patient is dead is very difficult job. Awareness about brain death is scarce in many parts of world therefore, it becomes more difficult is society or culture where common person lacking the knowledge. These families are always being doubt if anything more can be done to save life or to wake up the patient as they cannot accept that brain stem death is actual death and cessation of functions is irreversible. A very good counselling by one of member of intensive care unit who are primary care team for patient and a transplant coordinator is required at this stage. Though acceptance has increased in developed world in recent years, a survey done at Westmead Hospital, New South Wales in 1995 has shown that about 20 % of families of brain death persons continued to have doubts about their patient if he or she is actually dead, while another 66% even after acceptance of brain death as actual death felt them alive emotionally¹². Sometimes relatives of dying person are not aware of religious verdict about brain death and organ donation and thus refuse donation, making religion a ground. Religious views from different world religions will be discussed in short while in same article.

Finland was first European country who in 1971 adopted brain death as legal indicator of death. Kansas State in US has brought same legal act earlier¹³. In USA, there are differences in laws about brain death (not the definition as all states recognize it) in different states, some require specific regulations about cardio-pulmonary resuscitation, some would allow physician/ person with specified qualification to announce brain death. In New Jersey even if patient meeting criteria of brain death, would be announced dead only after cardio respiratory failure if patients' religious belief define so¹⁴.

In Indian parliament brain stem death was legalized in 1995¹⁵. The issue of brain death was first discussed in Iranian parliament in 1995 (although decree from prominent scholars were already issued but for the purpose of legalization) and then again in 1999 and finally the act of Deceased or Brain Dead person organ donation was passed in 2000¹⁶.

The Council of Islamic Jurisprudence accepted brain death as biological and legal death in 1986¹⁷. Many Muslim countries including Saudi Arabia, Kuwait, Lebanon, Malaysia, Indonesia have also legalized brain dead organ transplantation during these years while in Pakistan it was legalized in 2007¹⁸.

Some countries have legislation of 'opting out', which means if a person is brain dead in a hospital and a wish from him is not found then it is assumed as organ donor unless person has clearly made wish against organ donation. Spain had an opting out system and for many years had shown highest numbers of deceased organ transplants. Spanish model was reproduced by many countries including Italy, Croatia and Portugal¹⁹.

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This source of organ (from brain dead donors) remains a subject of controversies and doubt. First of all, a well informed consent need to be addressed. Even if dying person has made clear wishes to donate organs and/ or tissues in case of brain death, family needs to be involved and if they over rule the wishes then organs cannot be retrieved. If family understands what is brain death, is satisfied with efforts made to save their patient and allow organ donation without any coercion only then organs can be retrieved from brain dead donor.

There should be no monetary or any other kind of compensation involved in getting consent. After the diagnosis of brain death has been established treating team must allow time to family to clear their queries / doubts and discuss among themselves before signing the consent.

Treating team must respect cultural and religious beliefs of family. Transplant from brain dead donors provides beneficence to end organ failure patients. Justice can be done by offering organs to most suitable recipients. There is also utilitarian concept can be seen with brain dead organ donor benefiting many end organ failure patients as well as those requiring some tissues for their treatment.

Religious Views:

Judaism: In Judaism all the prohibitions are set aside if there is the possibility of what is called in Hebrew *Pikuach Nefesh*, the saving of a life. Every effort is made to save life, even if it means breaking the holiest of codes.

Most of the scholars of Jewish community would agree on the points that; What is not permitted is to take an active role in hastening death (Euthanasia). It is not permitted to do something that would kill a person through an act that one performs, but one can remove that which is simply preventing the process of death from occurring it is permissible to cease artificial ventilation, tube feeding, and water feeding if the person is just being kept alive in a state that is not really living at all.

The famous case of the Terri Schiavo, some of the Orthodox scholars felt that feeding through tubes was the normal process. The person was eating and therefore, to take that away would be an act that would bring about death, and they were reluctant to do it. The vast majority of scholars, Reform and Conservative, and some Orthodox, felt that because the person was not swallowing, which really constitutes eating, the nutrients and the water were simply in the same category as medicine, which can be withdrawn if it is an impediment to death²⁰. Thus when they agree upon brain death and withdrawal of supports they would allow organ donation from brain dead as this will be going to save many others life.

Christianity: Generally, supports organ donation as an altruistic act and leaves decision on individuals. The Church of England has stated organ donation as act of Christian duty²¹. Catholics Pope John Paul II said “we shall receive supreme reward from God according to the genuine and effective love we have shown to our neighbour” . Pope Benedict XVI use to carry donor card since 1970s²¹. Jehovah’ s Witness; who do not allow blood transfusion their view on organ transplant is complex as they allow organ transplant without blood transfusion and leave donation as individual decision²². In terms of brain death, the fundamental pertinent perspective in Christianity has to do with conception of personhood, which is largely derived from the Hebrew scripture, in the first biblical book and chapter the Genesis 1:26.

There seems to be broad agreement that the specialness of a person resides in the human brain, without which there can be no thoughts or emotions or relating. Once the person is brain dead these individuals could provide a source of still functioning organs to replace failed organs in other living people with intact brain function (and hence personhood)²⁰.

Islam: Majority of Muslim scholars and jurists (belonging to various schools) of Islamic law have brought up the principle of priority of saving human life and hence gave it more importance over any other argument. The Grand Mufti of Egypt, sanctioned corneal transplants from cadavers of unidentified persons and from those who make a will to donate upon their death (Fatwa No. 1084 dated April 14, 1959). His successor Sheikh extended the fatwa/ decree to other organs in 1966 (Fatwa No. 993). In 1973, the Grand Mufti, issued a fatwa allowing harvesting of skin from an unidentified corpse. In 1979, The Grand Mufti sanctioned cadaveric donors provided there was a will, a witness for the will, or the consent of the relatives of the deceased. In the case of unidentified

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corpses, an order from the magistrate should be obtained before harvesting organs (Fatwa No. 1323 dated December 3, 1979).

The most detailed decree on organ transplantation was that of the Fourth International Conference of Islamic Jurists held in Jeddah in February 1988 (Resolution No. 1). It endorsed all previous decrees on organ transplantation, clearly rejected any trading or trafficking of organs, and stressed the principle of altruism²³.

Quran differentiate between dying process and death and says:

“Then why do you not (intervene) when (the soul of a dying person) reaches the throat? And you at the moment are looking on, but We (i.e. Our angels who take the soul) are nearer to him than you, but you see not”²⁴. The irreversible loss of vital organs like brain stem and respiratory centre is dying process and death follows as a final event.

First Islamic country to perform organ transplant from brain dead was Iran, in 1964, later other Islamic countries after searching an answer to question whether brain death equals death in Muslim faith and culture started the practice in the 1980s²⁵.

The third Islamic Summit Conference held in Makkah al-Mukarramah, Saudi Arabia in January 1981 concluded that brain death is an acceptable criterion for determination of death, ruling that Islamic law allows declaration of death when all vital functions of the brain irreversibly cease and the brain begins to degenerate as witnessed by specialist physicians. A clear Decree was designed in another conference held in Jordan in October 1986²⁵. Organs for transplant can be retrieved after brain death and been practiced in majority Muslim countries.

Decree from Ayatullah Syed Roohullah Khomaini Al Mosavi:

In response to an *istifta* (religious question) regarding transplantation of organs from the brain dead his verdict was, “It is authorized to use organs such as heart, liver, etc. of a definite brain dead with permission of organ owner for transplantation if it is lifesaving for some other person”²⁶. Decree from Ayatullah Syed Ali Al Hussaini Khamenei: In response to an *istifta*, he responded “In such situation, there wouldn't be any problem using organs if someone's life is saved by transplanting the organ”²⁷. Decree from Ayatullah Makarem Shirazi: he has also permitted organ transplant from a brain dead patient if it is completely and definitely diagnosed to be irreversible²⁸.

Deceased organ transplantation in Pakistan:

History of deceased kidney transplant in Pakistan was created by Sindh Institute of Urology and Transplantation (SIUT) in January 1995, when an organ (kidney) donated as gift by the Euro Transplant Foundation which had been retrieved from a 14-year-old Dutch girl who died of cerebral haemorrhage. This kidney was successfully transplanted into a 24-year-old Pakistani female patient with kidney failure.²⁹ The same foundation further gifted 22 more kidneys which were transplanted at same institution. Meanwhile SIUT raised public awareness program widely on both print and electronic media which resulted in successful awakening of young mind of a Karachi university student who made a wish, while dining with family, to be deceased organ donor. After few months of making this wish this young man was travelling on his motor bike and got hit by a truck, landed in a hospital where he remained in ICU on mechanical ventilator and finally announced brain dead. His father approached physicians who were looking after this young man in ICU of this private hospital and expressed his concern about his dying son's organ preservation in form of donation, so the private hospital approached SIUT and first national deceased kidney transplant carried out in October 1998, both kidneys of dying young man transplanted to two young male end stage kidney failure patients (one still alive with well-functioning graft). Later trend was followed by a young female who was working as a nurse in a private hospital in Karachi and her kidneys were donated by her family after her brain death, in fulfilment of her wish, this was in 2005. Then in 2007 a pathologist practicing in Karachi made wish to donate kidneys and his two kidneys transplanted to patients on haemodialysis at SIUT. Another kidney donation came from young dying man from Islamabad in March 2010 (other kidney from same donor was transplanted at Islamabad). This made total 30 kidneys transplanted from deceased donors done at SIUT and one at Islamabad. One adolescent donated liver and transplant was carried out at Lahore.

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Armed forces institute of cardiology (AFIC) made serious effort for doing deceased heart transplant in end 2010 they were able to convince family of young man with brain death in ICU of DHQ hospital, dry run was done, retrieval team reached to DHQ hospital, but unfortunately female recipient with advanced cardiomyopathy who was hospitalized at AFIC had sudden cardiac arrest during shifting to operation room and could not revived (personal communication with commandant FIC that time).

Recently, sister of our colleague had desired donation in case of an event and her kidneys were transplanted to two end stage kidney failure patients after being diagnosed as a brain dead, in Lahore 2023.

The common people in Pakistan have some myths about religious restrictions about deceased organ donation, but this article has discussed actual recommendations from religious scholars from different faiths, with references.

Conclusion:

Organ transplant from deceased donors can address shortage of organs for transplant. There are two types of deceased donors; one brain dead and other with circulatory failure. Vitality of organs depends on early retrieval of organs after circulation has stopped. So with complete understanding between treating physicians and family of deceased when they agree upon donation only after heart beat has stopped, donor has been shifted to operating room soon after heart beating stops and procedure is hurried. Brain death is cessation of brain stem function and is an irreversible condition. After Brain death patients kept in intensive care units on mechanical ventilation, thus their heart is still pumping blood to other organs which can be kept functional with continuous circulation. These viable organs can be used for transplantation in people with end organ failure. There are many social, emotional and cultural issues related to this kind of organ retrieval, although procedure has been legalized in majority of world countries and has been allowed by religious scholars from different religions. The Social issues can lead to ethical dilemma in certain scenarios.

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