

The subclinical incidence of CTS in pregnancy: Assessment of median nerve impairment in asymptomatic pregnant women

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ABSTRACT

PURPOSE: The true incidence of pregnancy related carpal tunnel syndrome (PRCTS) is unknown. Most of the diagnoses of PRCTS are made based only on clinical symptoms. Here, we report a prospective controlled clinical trial assessing the electrophysiological changes in pregnant women to provide objective measure of the median nerve function. **METHODS:** Pregnant women in the third trimester (n=69) and age-matched non-pregnant women (n=40) asymptomatic for CTS were included in the study. Nerve conduction studies of the median and ulnar nerves across the carpal tunnel were bilaterally performed with the standard techniques. **RESULTS:** All the median sensory nerve conduction studies (amplitude, latency and velocity) performed from the ring finger and palmar region to wrist showed significant prolongation of median nerve conduction in the pregnant women compared with the control group (*p≤0.05). Median sensory nerve latencies from palmar branches to wrist were significantly longer in the pregnant group (**p<0.01). Sensory nerve action potential amplitudes recorded in the palmar region were smaller in the pregnant women (45.1μV) than in the control group (56.5μV). Ulnar motor and sensory conduction studies showed no significant difference between the pregnant women and the control group. According to the mean values of median nerve conduction velocity, 8 (11%) pregnant women were electrophysiologically diagnosed as CTS and four of these cases became symptomatic later during pregnancy or after delivery. **CONCLUSIONS:** Median nerve impairment occurs even in asymptomatic pregnant women. The electrophysiological characteristics of this impairment are defined and the pathophysiology of PRCTS is discussed. Electrophysiological evaluation is a tolerable and feasible technique for the early diagnosis of PRCTS.

Search Terms: pregnancy, carpal tunnel syndrome, electrophysiology, median nerve conduction

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment disorder, resulting from compression of the median nerve at the wrist where it courses deep to transverse carpal ligament. CTS has been recognized as a common complication of pregnancy (Heckman & Sassard, 1994).

The pathophysiology of pregnancy related CTS (PRCTS) has been mostly attributed to redistribution of fluids (Ekman-Ordeberg et al., 1987; Wand, 1990; Padua et al., 2001), even though some authors do not agree (Seror, 1998). Hormonal changes (Snell et al., 1980), tenosynovitis (Schumacher et al., 1985) and vulnerability of the peripheral nerves (Takayama, 1990) are other possible causes. Maternal age (Turgut et al., 2001), weight gain (McLennan et al., 1987), parity (Wand, 1989), smoking and alcohol (Padua et al., 2001) are factors reported to be related with CTS in pregnancy.

The true incidence of PRCTS is unknown and estimates in literature are discordant, varying from 0.34% (Stolp-Smith et al., 1998) to 62% (Padua et al., 2001), depending on the study design and the criteria for diagnosis. Up to 62% of pregnant women report hand symptoms in third trimester (Padua et al., 2001); however only a small number of these women undergo electrodiagnostic testing for assessment of median mononeuropathy (Weimer et al., 2002). Most published reports are based on subjective patient assessment (Finsen & Zeitlmann, 2006), clinical evaluations (Ekman-Ordeberg et al., 1987) or retrospective chart reviews (Stolp-Smith et al., 1998). There are limited data showing electrophysiological changes during pregnancy induced CTS (Padua et al., 2001). Since the diagnosis of CTS based solely on symptoms and signs is unreliable (Eogan et al., 2004), it is commonly accepted that only a neurophysiological evaluation provides objective data on the nerve function (Weimer et al., 2002).

CTS during pregnancy is usually considered by practitioners to be a benign condition which justifies reassurance as it is expected to resolve spontaneously after delivery. However, it can be very painful and can lead to disability as it is reported that 40% of PRCTS cases had residual signs of median nerve damage (two-point discrimination abnormality, thenar atrophy and weakness) after delivery (Wand, 1990). Since CTS can result in permanent disability if undiagnosed or left untreated (Wand, 1990), it is essential to recognize the syndrome when it occurs during pregnancy. In the present study, we evaluated to what extent pregnancy influences the electrophysiology of median nerve in women who have no complication of pregnancy or other predisposing factor for CTS. Sensitive electrophysiological tests were used to provide objective data about median nerve function during the third trimester of pregnancy. We also calculated the incidence of subclinical CTS in our sample with characteristics of electrophysiological investigations to determine the diagnostic criteria for predicting the syndrome earlier.

METHODS

Pregnant women in their third trimester who were receiving prenatal care at the maternity care clinics of our institute were routinely questioned for the inclusion criteria of our study. The study was approved by the local ethical committee. Following explanation of the aims and methods of the study, written informed consent was obtained from each subject who agreed to participate in the study. Symptomatic pregnant women detected during survey were excluded from the study, but referred to their obstetricians for further investigations and appropriate treatment.

Exclusion criteria were previous history of CTS, underlying disease such as rheumatoid arthritis, diabetes, gout, and hypothyroidism, space-occupying lesions such as a ganglion, previous fracture of the distal radius or possible work or cumulative trauma which are factors believed to predispose CTS. Pregnant women with complications of pregnancy, such as hypertension, preeclampsia and toxemia were

also excluded from the study since these conditions do not reflect physiological changes during pregnancy but are highly related with CTS caused by overweight and excessive edema.

The participants in the control group were age-matched asymptomatic women with normal nerve conduction parameters in both hands. All participants were questioned for the classical symptoms of CTS (pain, tingling) and were examined using clinical diagnostic tests for CTS (Tinnel's test, Phalen's test and the median nerve compression test). After these evaluations, sixty-nine uncomplicated pregnant and forty non-pregnant women asymptomatic for CTS were included in our study.

Electrodiagnostic evaluation

Electrodiagnostic tests included the conduction studies of median motor and sensory nerves across the carpal tunnel (amplitude, latency and velocity). As the ulnar nerve runs outside the flexor retinaculum, it is not subject to the same compressive forces as the median nerve; thus ulnar nerve conduction studies were carried out in order to use as a comparative standard and also to exclude patients with coincidental polyneuropathy or cervical radiculopathy.

Electrodiagnostic studies of the median and ulnar nerves were conducted bilaterally with the techniques described by Kimura (Kimura et al., 2001). The nerve was stimulated and a recording electrode detected the wave of depolarization as it passed by the surface electrode (either distally or proximally). The latency to the onset of action potential and the amplitude of signal were recorded for each sensory nerve. The tests were performed with the orthodromic supramaximal stimulation by a transcutaneous pulse of electricity inducing an action potential in the nerve over a distance of 14 cm, and a standard distance of 3 cm between electrodes were used. Hand temperature was recorded at the palm and was monitored at 33 °C or above. All studies were performed by the same neurophysiologist on Medelec Sapphire 4 ME machine (Medelec, Surrey, UK) at room temperature.

Statistical Analysis

Student's independent *t* tests were used to compare the means of electrophysiological variables between the pregnant and control groups. Throughout statistical analysis, the significance level was set at $p < 0.05$ with 95% confidence interval. All values are reported as a mean plus-or-minus the standard deviation.

RESULTS

Median and ulnar nerve conduction studies in pregnant women

One hundred-nine participants asymptomatic for CTS were recruited for our study, comprising sixty-nine pregnant women in third trimester with gestations ranging from 27 to 41 weeks and forty non-pregnant controls. We excluded the pregnant women with a history of any known cause and predisposing factors of CTS in order to estimate the real contribution of physiological changes into the median nerve function during pregnancy.

Since a number of factors influences peripheral nerve conduction velocity such as age and sex, we had a sex- and age-matched control group. When the mean ages of pregnant women (26 ± 5.8) and control group (25 ± 6.6) were compared, there was no statistically significant difference between these groups ($p > 0.05$). Twenty-four (35%) pregnant women were primigravid and 45 (65%) multigravid with parity ranging from 2 to 6.

The upper extremities bilaterally of the women in both pregnant (n=138) and control (n=80) groups were evaluated electrophysiologically. We have found that the median sensory nerve latencies were significantly longer in the pregnant group performed from 4th digital (*p<0.01) to wrist (Table 1) confirming that median sensory nerve studies with palmar stimulation have higher sensitivity compared to digital stimulation as reported before (Tireli et al., 1997).

Table 1: Median sensory nerve conduction studies in pregnant and control groups

Median Sensory Nerve	Conduction parameters (units)	Pregnant (n=138)	Control (n=80)	t	p
2 nd digit	latency(ms)	2.07±0.25	2.03±0.18	1.25	>0.05
	amplitude(μV)	30.7±11.5	32.1±9.7	-0.88	>0.05
	velocity(m/s)	51.3±4.0	53.1±3.3	-3.33	**<0.01
4 th digit	latency(ms)	2.05±0.24	1.98±0.21	2.05	*<0.05
	amplitude (μV)	29.5±12.4	31.7±14.9	-1.08	>0.05
	velocity(m/s)	51.2±4.58	52.4±3.3	-2.08	*<0.05
2 nd palmar	latency(ms)	1.55±0.19	1.47±0.16	2.82	**<0.01
	amplitude (μV)	46.3±15.3	60.9±18.9	-6.17	***<0.0001
	velocity(m/s))	48.5±4.3	49.3±2.52	-1.47	>0.05
3 rd palmar	latency(ms)	1.54±0.21	1.45±0.17	3.06	**<0.01
	amplitude (μV)	45.1±13.6	56.5±18.8	-5.12	***<0.0001
	velocity(m/s)	48.2±3.7	49.3±2.3	-2.54	*<0.05

Electrophysiological variables of median sensory nerve in pregnant and control groups. Median sensory nerve conduction values were obtained from the digits (second, fourth) and palmar (second, third) regions in both upper extremities of the pregnant and control groups as described in the methods section. The results are represented as mean value ± SD. P-values were calculated pregnant vs control (*p<0.05 **p<0.01 ***p<0.001).

The median sensory nerve action potential amplitudes recorded in palmar region were significantly smaller in the pregnant women (45.1±13.6) than in the control group (56.5±18.8) (***p<0.0001). The amplitude of compound action potential (8.84±1.63) and the median motor nerve conduction velocity between wrist and elbow (61.82± 7.02) were slightly smaller in the pregnant women compared to the control group but the difference was not statistically significant (p>0.05) (data not shown).

The assessment of ulnar motor and sensory nerve conduction studies confirmed that there was no significant difference between the pregnant and control groups (p>0.05) (Table 2). A comparison between primigravid and multigravid pregnant women did not show significant differences in electrophysiological measurements either (p>0.05) (data not shown).

Taken together, these results demonstrate that the median sensory nerve conduction across the wrist was significantly affected by pregnancy as the ulnar motor and sensory nerve conduction studies were normal, suggesting CTS.

Table 2: Ulnar motor and sensory nerve conduction studies in pregnant and control groups

Ulnar nerve	Conduction parameters (units)	Pregnant (n=138)	Control (n=80)	t	p value
Sensory					
5th digit	latency (ms)	1.77±0.31	1.78±0.15	0.95	>0.05
	amplitude (µV)	22.22±6.37	23.17±5.48	1.11	>0.05
	velocity (m/s)	51.03±7.22	51.54±2.46	0.36	>0.05
Motor					
wrist-elbow	wrist latency(ms)	2.11±0.23	2.18±0.44	-1.52	>0.05
	elbow latency	5.77±0.55	5.73±0.52	0.51	>0.05
	wrist amplitude(µV)	7.68±1.73	8.11±2.28	1.65	>0.05
	elbow amplitude	7.61±2.30	7.34±1.81	0.89	>0.05
	velocity (m/s)	60.87±5.96	60.89±6.12	-0.03	>0.05

Electrophysiological measures of ulnar sensory and motor nerves in pregnant and control groups. Ulnar sensory nerve conduction velocities were obtained from the fifth digit. Ulnar motor nerve conduction velocity calculated between wrist and elbow in both upper extremities of the pregnant and control groups as described in the method section. The results are represented as mean value ± SD. T and P values of the student t-test comparing the two groups are displayed as well (*p<0.05 **p<0.01 *p<0.001).**

Subclinical CTS in pregnancy

Median sensory nerve conduction velocities obtained from the digits and palmar regions were significantly smaller in the pregnant women (Figure1) which is evidence of a slowdown of median sensory nerve conduction.

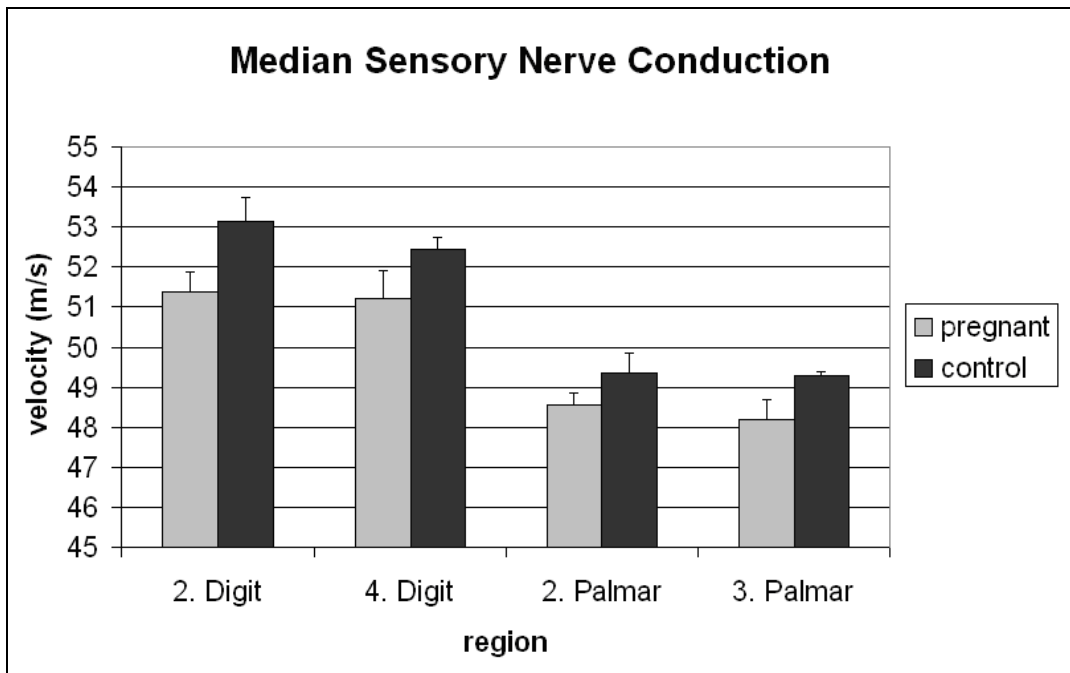


Figure 1: Median sensory nerve conduction changes across the carpal tunnel during pregnancy. Median sensory nerve conduction velocities were measured from different regions shown as mean values in pregnant and control groups. Error bars represent standard deviations

The $-2SD$ mean values of median sensory nerve conduction velocities obtained from the different regions in the control group were accepted as the lower limit for pathology. The median nerve conduction velocities below these limits in the pregnant group were represented as the pathological ratio. According to these limits, 15 participants in the pregnant group had the prolongation of median nerve conduction across the carpal tunnel by palmar stimulation (velocity $< 44.7\text{m/s}$). In eight of these participants, the findings were bilateral, and were diagnosed as mild CTS, representing the subclinical incidence of CTS in pregnancy. This corresponds to 11% of the pregnant group. Four of these cases (50%) developed CTS symptoms during the course of pregnancy or after delivery. Three of these cases required conservative therapy as one of them was operated after delivery due to severe symptoms. Other participants were not willing to participate in follow-up study.

DISCUSSION

In the present study, we have demonstrated that the median sensory nerve function was impaired in the pregnant women while the ulnar sensory nerve conduction remained unaffected. The electrophysiological responses are quite stable and reproducible and they reflect the physiologic health of the median nerve in the carpal tunnel (Kimura et al., 2001). Since a diagnosis of median mononeuropathy is based solely on the electrophysiologic measures of the median sensory function relative to ulnar sensory function, we conclude that pregnancy leads to entrapment of median nerve across the carpal tunnel even without symptoms. A possible explanation for the slowing of median nerve across the wrist without symptoms might be that the pathophysiologic abnormality occurs so insidiously that individuals are not aware and do not report the symptoms of numbness and tingling that is associated in acute CTS. It is known that slowing in electrophysiology may be primarily due to a thinning of the myelin sheath and/or a decrease in the distance between the nodes of Ranvier. Both changes are consistent with damage to the median nerve due to local compression (Werner & Andary, 2002).

The parity is found to be an important factor for CTS developed in puerperium and it is observed predominantly in older primigravid breastfeeding women (Snell et al., 1980; Wand, 1989). In a multicenter study of third trimester pregnant women, edema was found to be correlated with the electrophysiological picture in CTS, probably due to local compression (Padua et al., 2001). No correlation was observed with the number of previous pregnancies and CTS measurements in third trimester, which is consistent with our results .

Early-onset CTS (during first two trimesters of pregnancy) patients have the characteristic severe, rapidly progressive symptoms leading to failure of conservative treatment and most of them undergo surgery (Stahl et al., 1996; Seror, 1998). Nerve conduction studies of these cases demonstrated evidence of an acute median nerve lesion at the wrist with motor and/or sensory conduction blocks (Seror, 1998; Weimer et al., 2002). The acute or subacute flexor tenosynovitis is thought to contribute in these cases as corticosteroid injections provided very quick improvement both clinically and electrophysiologically. This shows that the pathophysiology is local ischemia due to acute compression of the nerve since the duration of the compression is positively correlated with the latency period needed for recovery after release of compressive force (Werner & Andary, 2002). In third trimester PRCTS, most CTS cases improve spontaneously without treatment, but in half of the women CTS symptoms disappear one year after delivery (Pazzaglia et al., 2005). This suggests a chronic course of pathophysiology due to edema in the third trimester which resolves after delivery. These reports, together with our results, strongly support the idea that the pathophysiology and characteristics of CTS developed in the third trimester are different than early-onset CTS or CTS developed in puerperium.

Sensitive electrophysiological methods are able to detect median nerve damage, even preceding clinical symptoms. Palmar stimulation has been described as a more sensitive and practical method in comparison with finger stimulation to detect even mild cases of CTS (Kimura, 2001). Our results confirmed the sensitivity of the palmar stimulation method since the pathology ratios in pregnant women were found to be 10.9% with the palmar and 8.7% with the digital stimulations.

Our electrophysiological investigations demonstrated that not only the prolongation of latency, but also the decreased SNAP amplitude and sensory nerve conduction velocity in pregnancy indicate a median mononeuropathy across carpal tunnel during pregnancy. Additionally, we found motor conduction velocity and CMAP amplitude slightly decreased. The exact cause of the decreased forearm median motor conduction velocity in CTS is still a subject of controversy. A conduction block or an axonal loss in the large myelinating fibers upon wrist compression, or retrograde axonal atrophy can be assumed. It has been reported that retrograde axonal atrophy and not selective damage to the large myelinating fibers at the wrist, is the direct cause of decreased forearm median motor conduction velocity in CTS (Chang et al., 2003). Retrograde axonal atrophy and relatively slowed median forearm motor conduction velocity do occur in CTS patients, regardless of severity of clinical manifestations and electrophysiological abnormalities (Chang et al., 2004), which is consistent with our findings in asymptomatic pregnant women. These abnormal conduction values seem to confirm a pre-clinical state of CTS, however a broad aspect follow-up study needs to be conducted to determine the electrophysiological criteria for the prediction of CTS earlier in pregnancy.

Using only the distal latency as an indicator for the nerve conduction, it has been reported that the conduction velocities of both median and ulnar nerves are affected by pregnancy, but only 72% of the sample of pregnant women were symptomatic (Eogan et al, 2004). In the study, asymptomatic pregnant women (n=5) had latencies similar to the control group and the ulnar nerve conduction was unexpectedly faster in the pregnant population than in the non-pregnant cohort of that sample. The authors did not propose possible explanations for the fast ulnar nerve conduction in the pregnant group. This might be a consequence of only the distal latencies being used for the assessment of nerve conduction. Our study is the first prospective controlled clinical study that performed the sensitive electrophysiological investigations to assess the median nerve conduction in asymptomatic pregnant women. Numerous studies have previously reported that the comparison of sensory nerve responses is more sensitive than the absolute median latency in documenting the electrodiagnostic abnormalities which indicate CTS (Werner & Andary, 2002). We have found that the median sensory nerve latency, action potential amplitude and conduction velocity were all affected in pregnancy, but not the ulnar nerve conduction studies as expected in CTS.

Only a small percentage of pregnant women are referred for electrodiagnostic testing, implying that CTS is not clinically suspected in most pregnant women with hand symptoms (Weimer et al., 2002). Thus, the incidence of untreated women with pregnancy-associated CTS is not known. Previous studies suggest that PRCTS requires serious attention from the obstetrician or practitioner, particularly if electrodiagnostic studies indicate a significant problem. Corticosteroid injection should be considered when electrodiagnostic studies indicate mild or moderate median nerve lesion with or without conduction block (Seror, 1998). Surgery is recommended when the motor latency is more than 5ms (Assmus & Hashemi, 2000). Taken together, electrophysiological studies remains an important means documenting possible CTS in pregnancy so that beneficial therapies can be implemented.

In conclusion, we have demonstrated that 11% of the third-trimester pregnant women in our sample have the objective evidence of abnormal median nerve conduction within the carpal tunnel, suggesting a subclinical entity associated with pregnancy induced CTS. We emphasize the importance of electrodiagnostic studies in pregnancy, especially due to their tolerability and feasibility, and suggest postpartum electrodiagnostic studies which would allow comparison with antenatal assessment. These

comparisons will provide further guidance as to where the physiological effects of pregnancy end and pathological carpal tunnel syndrome begins.

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